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## **Are there benefits from using bone-borne maxillary expansion instead of tooth-borne maxillary expansion? A systematic review with meta-analysis**

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**Abstract:** Background: The aim of the current systematic review was to compare the clinical effects of bone-borne or hybrid tooth-borne rapid maxillary expansion (RME) with conventional tooth-borne RME in the treatment of maxillary deficiency. Methods: Nine databases were searched up to September 2018 for randomized clinical trials comparing bone-borne or hybrid tooth-borne RME to conventional tooth-borne RME in patients of any age or sex. After duplicate study selection, data extraction, and risk of bias assessment with the Cochrane tool, random effects meta-analyses of mean differences (MD) and their 95% confidence intervals (CIs) were performed, followed by assessment of the quality of evidence with GRADE. Results: A total of 12 papers on 6 unique trials with 264 patients (42.4% male; average age 12.3 years) were finally included. Limited evidence indicated that bone-borne RME was associated with greater suture opening at the first molar post-retention (1 trial; MD 2.0 mm; 95% CI 1.4 to 2.6 mm; moderate evidence quality) compared to tooth-borne RME, while no significant differences could be found regarding tooth inclination, nasal cavity width, and root resorption (very low to low evidence quality). Hybrid tooth-borne RME was associated with less buccal tipping of the first premolar (2 trials; MD - 4.0°; 95% CI - 0.9 to - 7.1°; moderate evidence quality) and lower nasal airway resistance post-retention (1 trial; MD - 0.2 Pa s/cm<sup>3</sup>; 95% CI - 0.4 to 0 Pa s/cm<sup>3</sup>; moderate evidence quality) compared to tooth-borne RME, while no significant difference could be found regarding skeletal maxillary width, molar inclination, and analgesic use (low to moderate evidence quality). The main limitations affecting the validity of the present findings were (a) imprecision due to the inclusion of few trials with limited sample sizes that precluded robust detection of existing differences and (b) methodological issues of the included trials that could lead to bias. Conclusions: Limited evidence from randomized trials indicates that bone-borne or hybrid tooth-borne RME might present advantages in terms of increased sutural opening, reduced tooth tipping, and lower nasal airway resistance compared to conventional tooth-borne RME. However, the limited number of existing studies and issues in their conduct or reporting preclude the drawing of definite conclusions. Review registration: PROSPERO ( CRD42017079107 ). Keywords: Adverse effects; Clinical trials; Effectiveness; Maxillary expansion; Meta-analysis; Orthodontics; Skeletal anchorage; Systematic review.

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## **Title Page**

# **Are there benefits from using bone-borne maxillary expansion instead of tooth-borne maxillary expansion? A systematic review with meta-analysis**

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**Protocol and registration:** The protocol was registered prior to the study in the publicly assessable PROSPERO database (CRD42017079107).

**Availability of data and materials:** All data generated or analyzed during this study are included in this published article or its supplements, while its dataset is openly provided through Zenodo (<http://doi.org/10.5281/zenodo.1494107>).

**Authors' contributions:** The first and last authors (MK and SNP) performed study selection, data extraction, and risk of bias assessment independently and in duplicate. Literature search and data analysis were performed from the third author (SNP). Disagreements were resolved by discussion or the involvement of the second author (TE). All authors read and approved the final manuscript.

**Ethics approval and consent to participate:** Ethical approval was not required.

**Consent for publication:** Not applicable.

**Competing interests:** The authors declare that they have no competing interest.

## **Abbreviations**

CBCT: Cone Beam Computerized Tomography; CI: Confidence Interval; GRADE: Grading of Recommendations Assessment, Development and Evaluation; MD: Mean Difference; PICOS: Participants-Interventions-Comparisons-Outcome-Study design; RCT: Randomized Clinical Trial; REML: REstricted Maximum Likelihood; RME: Rapid Maxillary Expansion; RR: Relative Risk.

## Abstract

**Background:** Aim of the current systematic review was to compare the clinical effects of bone-borne or hybrid tooth-bone-borne rapid maxillary expansion (RME) with conventional tooth-borne RME in the treatment of maxillary deficiency.

**Methods:** Nine databases were searched up to September 2018 for randomized clinical trials comparing bone-borne or hybrid tooth-bone-borne RME to conventional tooth-borne RME in patients of any age or sex. After duplicate study selection, data extraction, and risk of bias assessment with the Cochrane tool, random effects meta-analyses of Mean Differences (MD) and their 95% confidence intervals (CIs) were performed, followed by assessment of the quality of evidence with GRADE.

**Results:** A total of 12 papers on 6 unique trials with 264 patients (42.4% male; average age 12.3 years) were finally included. Limited evidence indicated that bone-borne RME was associated with greater suture opening at the 1<sup>st</sup> molars post-retention (1 trial; MD: 2.0 mm; 95% CI: 1.4 to 2.6 mm; moderate evidence quality) compared to tooth-borne RME, while no significant differences could be found regarding tooth inclination, nasal cavity width, and root resorption (very low to low evidence quality). Hybrid tooth-bone-borne RME was associated with less buccal tipping of the 1<sup>st</sup> premolar (2 trials; MD: -4.0°; 95% CI: -0.9 to -7.1°; moderate evidence quality) and lower nasal airway resistance post-retention (1 trial; MD: -0.2 Pa s/cm<sup>3</sup>; 95% CI: -0.4 to 0 Pa s/cm<sup>3</sup>; moderate evidence quality) compared to tooth-borne RME, while no significant difference could be found regarding skeletal maxillary width, molar inclination, and analgesic use (low to moderate evidence quality). The main limitations affecting the validity of the present findings were (a) imprecision due to the inclusion of few trials with limited sample sizes that precluded robust detection of existing differences and (b) methodological issues of the included trials that could lead to bias.

**Conclusions:** Limited evidence from randomized trials indicates that bone-borne or hybrid tooth-bone-borne RME might present advantages in terms of increased sutural opening, reduced tooth tipping, and lower nasal airway resistance compared to conventional tooth-borne RME. However, the limited number of existing studies and issues in their conduct or reporting preclude the drawing of definite conclusions.

**Keywords:** orthodontics, maxillary expansion, skeletal anchorage, effectiveness, adverse effects, clinical trials, systematic review, meta-analysis



# MANUSCRIPT

## Introduction

Transverse maxillary deficiency is a malocclusion seen among adolescents or adults with prevalence over 8%-10% [1, 2] and can manifest clinically as unilateral or bilateral crossbite, narrow nasal cavity, arch length discrepancy, and crowding [3, 4]. Additionally, some evidence indicates that posterior crossbites might be associated with temporomandibular disorders, including clicking and muscle tenderness [5]. Therefore, transverse maxillary deficiencies are usually treated on diagnosis to enable the settling of a harmonic occlusion, while avoiding any potential side-effects.

In the treatment of transverse maxillary deficiencies, especially among adolescents, orthopedic expansion of the maxilla along the median palatal suture holds a prominent place [6]. This usually follows the protocol of a Rapid Maxillary Expansion (RME), where the palatal expander is fixed on the maxillary posterior teeth. RME using tooth-borne expanders has been shown to be an effective alternative for the treatment of maxillary transverse deficiency [7] among adolescents with treatment effects including an expansion of the maxillary arch (being mostly dental and less skeletal [8,9]), widening of the nasal cavity [10], anterior movement of the maxilla [11] with a downward rotation [12], and a small spontaneous increase in mandibular arch width [9]. On the other side, tooth-anchored RME has also been associated with some adverse effects to the teeth and the surrounding tissues, including among others buccal tooth tipping [11], reduced buccal bone thickness [13], marginal bone loss [13], bone fenestration [14], buccal gingival recessions [15], and root resorption [16].

In order to overcome these potential limitations and possibly enhance the skeletal effects of conventional tooth-borne RME, the use of an RME anchored completely or partly on skeletal anchorage devices was proposed [17], designated as bone-borne or hybrid (tooth-bone-borne) RME, respectively. The suggested benefits of such appliances include greater skeletal expansion of the maxilla and facial bones, reduced burden and adverse effects on the anchorage teeth, and improved stability of the results. These benefits come of course at the cost of increased invasiveness of the procedure and increased risk of wound infection [18].

Even though research on this field continues to increase, clinical evidence about the comparative performance of skeletally anchored RME has not been systematically and critically appraised. Therefore,

aim of the present systematic review was to compare the efficacy and adverse effects of partially/completely skeletally anchored RME versus conventional (tooth-borne) RME for the treatment of maxillary transverse deficiency based on evidence from randomized clinical trials.

## **Material and methods**

### **Protocol, eligibility criteria, and registration**

This review's protocol was made a priori, registered in PROSPERO (CRD42017079107), and all post hoc changes were appropriately noted. This systematic review was conducted and reported according to Cochrane Handbook [19] and Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [20], respectively.

Based on the Participants-Interventions-Comparisons-Outcome-Study design (PICOS) approach, we included randomized controlled clinical trials on human patients of any age or sex with transverse maxillary deficiency treated with bone-borne compared to tooth-borne maxillary expansion in terms of skeletal expansion as the primary outcome. Two discreet experimental interventions were considered eligible and compared with the conventional tooth-borne RME control: purely bone-borne RME, as well as hybrid tooth-bone-borne RME. Non-randomized studies, animal studies, in vitro studies, and studies, where RME was surgically assisted, were excluded.

### **Information sources and literature search**

The following nine electronic databases were systematically searched for this review: MEDLINE (via PubMed), Embase, The Cochrane Library (CDSR, CENTRAL, and DARE), Virtual Health Library (including Bibliography Brazilian Dentistry and LILACS), Scopus, ISI Web of Knowledge, and ClinicalTrials.gov (Appendix 1). Manual searches were applied on the databases Directory of Open Access Journals (DOAJ), Digital Dissertations (via UMI Proquest), metaRegister of Controlled Trials, WHO trials search portal, and Google Scholar for additional trials as well as for the reference lists of the included studies. The entire search was made by one author (SNP) without any limitations from inception of each database up to September 29<sup>th</sup>, 2018. Aside from filtering trials on humans, no other filters for language, publications year, and status were applied.



**Study selection and data collection,**

The identified studies from the literature search were sequentially screened by title, abstract, and full text by one author (MK) with subsequent duplicate independent checking against the eligibility criteria by another author (SNP), while conflicts were resolved by a third author (TE).

The same protocol was applied for the extraction of study characteristics (study design, setting, country, patient number, sex, age, appliances, treatment duration, timing of follow-up, activation protocol, measurement method, and outcome measured) and for the numerical data collection using pre-defined forms. Piloting of the forms was performed during the protocol stage until over 90% agreement was reached. When any data was missing in the trial, it was calculated from existing data or the corresponding author was contacted.

**Risk of bias in individual studies**

The risk of bias within the individual included randomized studies was evaluated using the Cochrane risk of bias tool [19]. This assessment was performed by one author (MK) and independently checked by another author (SNP).

**Data synthesis**

The primary outcome of this systematic review was the difference in the achieved amount of skeletal maxillary expansion between bone-borne or hybrid tooth-bone-borne RME and conventional tooth-borne RME. Secondary outcomes included dental positional / inclination changes, other skeletal changes, root resorption, structural / functional airway measurements, and patient-reported outcomes.

Data were summarized and considered suitable for pooling, if similar intervention and/or control groups were compared and if similar outcomes were reported. All existing trials were included in the analysis independently of reporting completeness, if possible; where data was missing, they were calculated from existing data or requested them from the authors. For studies reporting on data before and after treatment, but not on the treatment-induced changes, we calculated those with a moderate pre-post correlation of 0.75.

Mean Differences (MDs) of treatment changes for continuous outcomes and Relative Risks (RRs) for binary outcomes and their corresponding 95 % confidence intervals (CIs) were calculated. The standardized mean difference was also chosen *post hoc* to combine two similar measurements of nasal cavity width into a single meta-analysis (Appendix 2). As the effects of RME were deemed to be highly variable according to patient age, sex, and individual variation of the maxillofacial sutures, a random-effects model was chosen over a fixed-effect one to calculate the average distribution of treatment effects that can be expected [21]. A REstricted Maximum Likelihood (REML) random-effects variance estimator was used instead of the older DerSimonian-Laird one, following recent guidance [22]. Random-effects 95% predictions were calculated for meta-analyses with at least three studies to aid in their interpretation by quantifying expected treatment effects in a future clinical setting [23].

The extent and impact of between-study heterogeneity were assessed by inspecting the forest plots and by calculating the tau-squared and the I-squared statistics, respectively. The 95 % CIs (uncertainty intervals) around tau-squared and I-squared were calculated to judge our confidence about these metrics. We arbitrarily adopted the I-squared thresholds of >75% to be considered as signs of considerable heterogeneity, but we also judged the evidence for this heterogeneity (through the uncertainty intervals) and the localization on the forest plot.

A two-tailed P-value of 0.05 was considered significant for all hypothesis-testing, except for a 0.10 used for the test of heterogeneity and reporting biases. All analyses were run in Stata SE 14.0 (StataCorp, College Station, TX) by one author (SNP) and the study's dataset was openly provided [24].

### **Risk of bias across studies and additional analyses**

Subgroup analyses, meta-regressions, assessments of reporting biases, and sensitivity analyses were initially planned in the review's protocol, but could ultimately not be conducted due to limited number of included trials (Appendix 2).

The overall quality of clinical recommendations (confidence in effects estimates) for each of the main outcomes was rated by using the Grades of Recommendation, Assessment, Development, and Evaluation (GRADE) approach [25] using an improved Summary of Findings table format [26]. The optimal information size was estimated for each outcome independently to be able to identify a minimal clinical

important effect with an average standard deviation (based on this review's study sample), with type I and type II errors set at 5% and 20%, respectively. The minimal clinically important, large, and very large effects were conventionally defined as half, one, and two standard deviations for continuous outcomes [27] and as relative risks of 1.5, 2.5, or 5.0 for binary outcomes [28]. This assessment of the risk of bias for among-trials was conducted independently by two authors (SP and MK) and discrepancies were resolved.

## **Results**

### **Study selection**

The electronic literature yielded a total of 622 records, while 3 more were identified manually (Figure 1). After removal of duplicates and screening of titles and abstracts, 113 full-text papers were scrutinized against the eligibility criteria. After applying the eligibility criteria, a total of 12 publications pertaining to six unique RCTs were finally included in this systematic review (Appendix 3).

### **Study characteristics**

The six included RCTs were conducted in clinics, private practices, or university clinics in four different countries (Canada, Netherlands, Sweden, Turkey) and had been published as journal papers and/or dissertations in English between 2009-2018 (Table 1a). As far as experimental groups are concerned, two trials included a pure bone-borne RME, three included a hybrid tooth-bone-borne RME, and one included both. The different designs of RME appliances used can be seen in Appendix 4. As far as control groups are concerned, all six trials included a conventional tooth-borne RME, while one trial also included an untreated control group that was disregarded, as it fell outside the scope of this review. These six trials included a total of 264 patients randomized into experimental or control groups with an average group size of 19 patients. From these 264 patients 112 (42.4%) were male and the average age across trials was 12.3 years. All trials used similar RME activation protocols, which included 2 turns of the expansion screw per day until (over-)correction of the maxillary deficit.

As far as outcome measurement is concerned (Table 1b), one trial assessed patient-reported outcomes during the first expansion days, three trials assessed outcomes directly post-expansion, and four trials assessed outcomes after an additional retention/observation period. A wide variety of outcomes were

measured by Cone Beam Computerized Tomography (CBCT) (4 trials), rhinomanometry (2 trials), plaster cast models (1 trial), and questionnaires (1 trial).

### **Risk of bias within studies**

The risk of bias of included trials ranged between low (one trial), unclear / low (two trials), and high (three trials). The most frequent reason for assigning a high risk for bias was the lack of blinding for the outcome measurement (three trials), followed by a potentially inadequate generation of the randomization sequence (one trial) (Figure 2; Appendix 5).

### **Results of individual studies & synthesis of results**

The results of every extracted outcome from each included randomized trial are given in Appendix 6a for the comparison of bone-borne versus tooth-borne expanders and in Appendix 6b for the comparison of hybrid (tooth-bone-borne) versus tooth-borne expanders. Only statistically significant and clinically relevant differences are given here, which pertain to results of single trials, unless meta-analyses are available, where they are reported as such and given in Table 2.

#### *Bone-borne compared with tooth-borne rapid maxillary expansion*

As far as differences directly post-expansion are concerned (Appendix 6a), only some dental positional / inclinational significant differences were reported from a single trial. As such, bone-borne RME was associated with less dental expansion at the canine (MD: -0.7 mm; 95% CI: -1.0 to -0.4 mm), less buccal tipping at the 1<sup>st</sup> premolar (MD: -4.3°; 95% CI: -6.9 to -1.6°), and less buccal tipping at the 1<sup>st</sup> molar (MD: -5.4°; 95% CI: -8.0 to -2.7°) compared to tooth-borne RME. Additionally, a meta-analysis of two trials indicated that bone-borne RME was associated with less buccal tipping of the 1<sup>st</sup> premolar (MD: -4.1°; 95% CI: -6.0 to -2.1°).

As far as data after a retention/observation period post-expansion are concerned (Appendix 6a), several skeletal maxillary, dental positional / inclinational, and nasal cavity clinically relevant differences were identified. One trial indicated that bone-borne RME was associated with (i) greater skeletal expansion at the incisal foramen (MD: 1.8 mm; 95% CI: 1.3 to 2.3 mm), (ii) greater suture opening at the 1<sup>st</sup> premolar

(MD: 2.3 mm; 95% CI: 1.7 to 2.9 mm), and (iii) greater suture opening at the 1<sup>st</sup> molar (MD: 2.0 mm; 95% CI: 1.4 to 2.6 mm) than tooth-borne RME. Three different single trials provided evidence that bone-borne RME was associated with (i) less intercanine width expansion (MD: -0.5 mm; 95% CI: -1.0 to -0.1 mm), (ii) less inter-1<sup>st</sup>-premolar width expansion (MD: -1.8 mm; 95% CI: -2.7 to -0.9 mm), (iii) less buccal inclination of the 1<sup>st</sup> premolar (MD: -5.1°; 95% CI: -6.8 to -3.4°), (iv) less buccal inclination of the 1<sup>st</sup> molar (MD: -5.2°; 95% CI: -7.0 to -3.5°), and (v) greater buccal bone thickness at the 1<sup>st</sup> premolar (MD: 0.3 mm; 95% CI: 0.1 to 0.4 mm) than tooth-borne RME. Additionally, bone-borne RME was associated with greater expansion of the nasal cavity width at the 1<sup>st</sup> molar (MD: 1.7 mm; 95% CI: 0.8 to 2.6 mm) than tooth-borne RME. Finally, no clinically relevant differences regarding skeletal vertical dimension, mandibular dimensions, or root resorption were observed.

#### *Hybrid (tooth-bone-borne) compared with tooth-borne rapid maxillary expansion*

As far as differences directly post-expansion are concerned (Appendix 6b), only one trial indicated that hybrid RME was associated with less intercanine width expansion (MD: -0.7 mm; 95% CI: -0.9 to -0.4 mm) compared to tooth-borne RME.

As far as differences after a retention/observation period are concerned, one trial indicated that hybrid RME was associated with (i) less inter-1<sup>st</sup>-premolar width expansion (MD: -4.3 mm; 95% CI: -7.0 to -1.6 mm), (ii) less inter-2<sup>nd</sup>-premolar width expansion (MD: -3.3 mm; 95% CI: -6.2 to -0.5 mm), (iii) greater buccal bone thickness at the 1<sup>st</sup> premolar (MD: 0.8 mm; 95% CI: 0.3 to 1.3 mm), and (iv) lower palatal bone thickness at the 1<sup>st</sup> premolar (MD: -1.6 mm; 95% CI: -2.2 to -1.0 mm) than tooth-borne RME. Finally, one meta-analysis of 2 trials indicated that hybrid RME was associated with less buccal tipping of the 1<sup>st</sup> premolar (MD: -4.0 mm; 95% CI: -7.1 to -0.9 mm) than tooth-borne RME.

#### **Risk of bias across studies and additional analyses**

No formal assessment of risk of bias across studies or any subgroup / sensitivity analyses could be performed due to the limited number of included trials in the meta-analyses, which would be rendered instable by trial omissions.

The quality of evidence for the comparison of bone-borne versus tooth-borne RME varied between very low and moderate (Table 3a). Moderate quality of evidence supported the greater sutural opening at the 1<sup>st</sup> premolar and the 1<sup>st</sup> molar, low quality of evidence backed the change in nasal cavity width or root resorption, while very low quality of evidence supported dental tipping changes during RME. The main reasons for downgrading were (i) the imprecision due to inadequate sample sizes of all trials, (ii) bias due to lack of outcome measurement blinding and inadequate randomization sequence generation, and (iii) inconsistency due to high heterogeneity.

The quality of evidence for the comparison of hybrid tooth-bone-borne versus tooth-borne RME varied between low and moderate (Table 3b). Apart from the change in the external maxillary skeletal width that was supported by low quality of evidence, all other comparisons were backed by moderate quality of evidence. The main reasons for downgrading were (i) the imprecision due to inadequate sample sizes of all trials and (ii) bias due to lack of outcome measurement blinding and inadequate randomization sequence generation.

## **Discussion**

### **Summary of evidence**

The present systematic review summarizes and critically appraises evidence from randomized clinical trials on the potential benefits of partly or completely skeletally anchored RME compared to conventional RME and is to our knowledge the first review to do so. A total of 12 publications pertaining to six unique trials including a total of 264 patients in need of RME were finally included in the analyses. The quality of recommendations that can be drawn from existing evidence according to the GRADE approach varies between very low to moderate, as all are based on few trials with mostly inadequate sample sizes and some trials have methodological limitations. This means that our confidence in these recommendations is hampered and future trials might change these provisional recommendations.

The idea behind using skeletal anchorage for RME is that greater skeletal expansion of the maxilla could theoretically be obtained. This systematic review found that bone-borne RME was associated with greater opening of the maxillary suture at the incisal foramen (1.8 mm more), first premolars (2.3 mm more) and the first molars (2.0 mm more) compared to conventional RME (Appendix 6a). This might be explained

by a direct force application to the maxilla, which leads to separation of the median suture and displacement of the two maxillary halves [29]. Sutural opening was not assessed for hybrid RME in any of the identified trials. Interestingly, no significant increase in the external buccal maxillary width at the 1<sup>st</sup> molars of either bone-borne ( $P=0.22$ ; Appendix 6a) or hybrid RME ( $P=0.54$ ; Appendix 6b) was seen compared to conventional RME. This might be attributed to either bone remodeling or alveolar bending [18].

At the same time skeletally-anchored RME is proposed over tooth-borne RME by many as a means of reducing the adverse effect of buccal tipping of the anchorage teeth. Evidence from the present review was inconclusive on whether bone-borne or hybrid RME could prevent buccal tooth tipping to a clinically meaningful degree. Even though the effects for the 1<sup>st</sup> premolar or 1<sup>st</sup> molar for both types of skeletally anchored RMEs were  $< 0$  (indicating less tipping than conventional RME), this was mostly not statistically significant (Table 2). However, caution is warranted in the interpretation of these findings, since this might be attributed to the limited number of trials with small sample sizes and heterogeneous results or to the fact that studies measured this outcome separately for right and left teeth. An indirect way to measure maxillary expansion in conjunction with tooth tipping might be to look at the buccal bone thickness at the 1<sup>st</sup> premolars and the 1<sup>st</sup> molars. Here, evidence from one trial [30] indicated that bone borne RME was associated with significantly greater buccal bone thickness at the 1<sup>st</sup> premolar and 1<sup>st</sup> molar (0.14 mm and 0.25 mm, respectively; Appendix 6a) compared to conventional tooth-borne RME. On the other side, data on buccal bone thickness after hybrid RME were more inconclusive, indicating greater bone thickness at the 1<sup>st</sup> premolar (0.63 mm more), but not the 1<sup>st</sup> molar (Appendix 6b) [18]. This might be attributed to the fact that the hybrid RME appliance was anchored on the 1<sup>st</sup> molars, but not the 1<sup>st</sup> premolars. When analyzing dental tipping after RME it is important to bear in mind the pyramid- or triangle-shaped opening of the suture due to the two centers of rotation, which leads to bending of the alveolar bone and subsequent tipping of the teeth [18, 31]. Therefore, there are some indications that tipping of the anchorage teeth might be influenced by anchorage type, although further evidence is needed to consolidate these.

Another outcome often measured in trials comparing bone-borne or hybrid RME to conventional RME is the dental arch width – usually at the 1<sup>st</sup> premolars or the 1<sup>st</sup> molars. Existing data indicated no significant difference in these dental arch width for either skeletally anchored RME compared to conventional RME ( $P>0.05$ ; Table 2). However, this is to be expected, since the most widely used criterion

to terminate RME was clinically determined when the upper palatal molar cusps touched the lower molar buccal cusps.

Several studies have reported increased width of the nasal cavity post expansion, which seems to be associated with the opening of the midpalatal suture [17, 32]. Evidence from a trial included in the present review indicated that bone-borne RME was associated with increased nasal cavity width at the 1<sup>st</sup> molar (by 1.7 mm; Appendix 6a) compared to conventional RME [30]. Additionally, data from another trial indicated that hybrid RME was associated with increased nasal airflow (by 57.7 cm<sup>3</sup>/s; Appendix 6b) and reduced nasal airway resistance (by -0.2 Pa s/cm<sup>3</sup>; Appendix 6b) compared to conventional RME [33]. Although it has been shown that RME in general might potentially increase the volume of the upper airways [34], the effect to which this contributes in improved breathing or quality of life is unclear. It must be noted here that based on current evidence no recommendations can be made for the use of any kind of RME for the treatment of breathing disorders like obstructive sleep apnea [35].

Another side-effect of RME that could potentially be alleviated using skeletal anchorage is the iatrogenic root resorption of the premolars and molars used as anchorage for the RME appliance [16]. Two trials included in the present review using bone-borne RME found no considerable differences in either linear or volumetric root resorption compared to conventional RME [30, 36].

Finally, as patient reported outcomes are concerned, only one trial existed that compared the short-term effect on the pain and discomfort during the first week of RME with a hybrid and a conventional appliance [37]. The results indicated that no significant differences exist in the pain or discomfort and analgesic consumption, apart from pain from molars / incisors and tensions from the jaw on day 4, where the hybrid RME group reported less disturbances than the conventional RME group.

### **Strengths and limitations**

The strengths of this systematic review consist of the registration of its a priori protocol in PROSPERO [38, 39], its exhaustive literature search, its improved analytical methods [22], the use of the GRADE approach [25] to assess the quality of the meta-evidence, and the transparent provision of the study's data [24, 40].

However, certain limitations also exist. First and foremost, although only randomized trials were included that are generally less prone to bias than non-randomized trials [41], many of them had



methodological limitations that might lead to bias [42]. Furthermore, the identified studies were predominantly small and this might introduce small-study effects [43]. Finally, the limited number of included studies and their suboptimal reporting did not enable assessments of heterogeneity, as well as the conduct of several analyses for subgroup subgroups (including among others different implant placement regions and different RME appliances), small-study effects, and reporting biases that were planned to assess the robustness of the analyses [44].

## **Conclusions**

Existing evidence from randomized trials on RME for transverse maxillary deficit indicates that bone-borne RME might be associated with greater skeletal maxillary expansion post-retention compared to tooth-borne RME, while no significant differences could be identified for a buccal tooth tipping, nasal cavity width, and root resorption. Hybrid tooth-bone-borne RME was associated with less patient discomfort during the first days of activation, less buccal tipping of the 1st premolar and lower nasal airway resistance post-retention compared to tooth-borne RME, while no significant differences could be found regarding skeletal maxillary width, molar inclination, and analgesic use. Overall, there exist some indications of potential benefits from partially or completely skeletally anchored RME, but only a few trials with very limited sample sizes and some risk of bias exist, which hampers our confidence in drawing clinical recommendations. Future well-designed randomized trials with a priori sample size calculation and blinded assessment of skeletal, dental, and breathing-related outcomes are needed.

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## Tables

**Table 1a.** Characteristics of included randomized trials pertaining to setting, patients, and intervention.

Study	Design; Setting; Country\$	Patients (M/F); Age*	Intervention; duration#	Activation protocol
Bazargani 2018	RCT; Clinic; SWE	EG1: 19 (11/8); 9.7 EG2: 21 (10/11); 10.2	EG1: TB RME; NR EG2: Hybr. RME; NR	2x/day until upper palatal molar cusps touch lower molar buccal cusps
Canan 2017	RCT; Uni; TUR	EG1: 16 (8/8); 12.6 EG2: 16 (7/9); 12.9 EG3: 15 (7/8); 13.4	EG1: TB RME; 13.3 d EG2: BB RME; 12.4 d EG3: Hybr. RME; 14.1 d	2x/day
Celenk-Koca 2018	RCT; Pract; NLD	EG1: 20 (8/12); 13.8 EG2: 20 (7/13); 13.8	EG1: TB RME; 19.7 d EG2: BB RME; 19.7 d	2x/day until upper palatal molar cusps touch lower molar buccal cusps
Feldmann 2017	RCT; Clinic; SWE	EG1: 25 (12/13); 9.7 EG2: 25 (12/13); 10.0	EG1: TB RME; NR EG2: Hybr. RME; NR	2x/day until upper palatal molar cusps touch lower molar buccal cusps
Gunyuz Toklu 2015	RCT; Uni; TUR	EG1: 13 (5/8); 14.3 EG2: 12 (6/6); 13.8	EG1: TB RME; 19.2 d EG2: Hybr. RME; 20.2 d	2x/day until upper palatal molar cusps touch lower molar buccal cusps
Lagravere 2009 <sup>collated†</sup>	RCT; Uni; CAN	EG1: 20 (5/15); 14.1 EG2: 21 (8/13); 14.2 CG: 21 (6/15); 12.9	EG1: TB RME; NR EG2: BB RME; NR CG: Observation	2x/day for DME (or 1x/2 days for the SME) until overcorrection

# duration of active transverse expansion in weeks

\$ countries are given with their ISO-3 code

\* Age is given in years either as mean (one value) or if mean not provided as range (two values in parenthesis)

† including the publications Lagravere 2010, Lagravere 2013, Kabalan 2015, Stepanko 2016 and the dissertations Lagravere 2009, Forst 2015

BB, bone-borne; CG, control group without expansion; EG, experimental group with expansion; F, female; Hybr., hybrid (tooth-bone-borne); RCT, randomized clinical trial; HME, hybrid (skeletally/dentally)-anchored maxillary expansion; M, male; NR, not reported; Pract, practice; RME, rapid maxillary expansion; SME, skeletally-anchored maxillary expansion; TB, tooth-borne; Uni, university.

**Table 1b.** Characteristics of included randomized trials pertaining to follow-up and outcome.

Study	Follow-up	Method/ outcome
Bazargani 2018	Post-exp	Rhinomanometry <ul style="list-style-type: none"> <li>▪ Nasal airflow</li> <li>▪ Nasal resistance</li> </ul> Plaster casts <ul style="list-style-type: none"> <li>▪ Dental arch width (IMW)</li> </ul>
Canan 2017	<ul style="list-style-type: none"> <li>• Post-exp</li> <li>• 6.0 mos post-exp</li> </ul>	CBCT <ul style="list-style-type: none"> <li>▪ 3D tooth movements</li> <li>▪ Dental arch width (ICW, IP1W, IMW)</li> <li>▪ Dental tipping (P1, M)</li> </ul> Clinical <ul style="list-style-type: none"> <li>▪ Technical complications</li> </ul>
Celenk-Koca 2018	<ul style="list-style-type: none"> <li>• 6.0 mos post-exp</li> </ul>	CBCT <ul style="list-style-type: none"> <li>▪ Dental arch width (IP1W, IMW)</li> <li>▪ Dental tipping (P1, M)</li> <li>▪ Root resorption</li> <li>▪ Skeletal maxillary width</li> <li>▪ Skeletal sutural opening amount &amp; pattern</li> </ul>
Feldmann 2017	1 <sup>st</sup> /4 <sup>th</sup> exp day	Questionnaire <ul style="list-style-type: none"> <li>▪ Pain</li> <li>▪ Discomfort</li> <li>▪ Jaw function</li> <li>▪ Analgesic consumption</li> </ul>
Gunyuz Toklu 2015	3.0 mos post-exp	CBCT <ul style="list-style-type: none"> <li>▪ Facial width</li> <li>▪ Skeletal maxillary width</li> <li>▪ Buccal/palatal bone thickness (C, P1, P2, M)</li> <li>▪ Alveolar (P1, M) / dental (C, P1, P2, M) tipping</li> <li>▪ Dental arch width (ICW, IP1W, IP2W, IMW)</li> </ul>
Lagravere 2009 <sup>collated†</sup>	<ul style="list-style-type: none"> <li>• Post-exp</li> <li>• 6.0 mos post-exp</li> <li>• 12.0 mos post-exp</li> </ul>	CBCT <ul style="list-style-type: none"> <li>▪ Nasal width</li> <li>▪ Skeletal maxillary width</li> <li>▪ Skeletal mandibular width</li> <li>▪ Dental arch width (IP1W, IMW)</li> <li>▪ Sagittal / vertical tooth movements (I, M)</li> <li>▪ Sagittal / vertical skeletal mandibular position</li> </ul> Questionnaire <ul style="list-style-type: none"> <li>▪ Pain</li> </ul> Acoustic rhinometry <ul style="list-style-type: none"> <li>▪ Nasal airway volume</li> </ul>

# duration of active transverse expansion in weeks

\$ countries are given with their ISO-3 code

\* Age is given in years either as mean (one value) or if mean not provided as range (two values in parenthesis)

† including the publications Lagravere 2010, Lagravere 2013, Kabalan 2015, Stepanko 2016 and the dissertations Lagravere 2009, Forst 2015

CBCT, cone beam computed tomography; Exp, expansion; I, incisor; IMW, intermolar width; IP1W, inter-(first)-premolar width; M, molar; P1, first premolar; P2, second premolar.



**Table 2.** Results of random-effects meta-analyses performed from randomized trials comparing tooth-borne rapid maxillary expansion with either bone-borne or hybrid (tooth-bone-borne) rapid maxillary expansion.

Experimental	Timing	Outcome	Trials	MD	95% CI	P	I <sup>2</sup> (95% CI)	tau <sup>2</sup> (95% CI)	95% PrI
Bone-borne	Pst-Exp	Intermolar width (crown)	2	-0.09	-0.34, 0.16	0.46	0% (0%, 98%)	0 (0, 8.14)	NC
Bone-borne	Pst-Exp	Inter-1 <sup>st</sup> -premolar width (crown)	2	-0.71	-2.70, 1.27	0.48	91% (41%, 100%)	1.88 (0.12, 258.72)	NC
Bone-borne	Pst-Exp	Inclination 1 <sup>st</sup> molar (left)	2	-2.93	-7.87, 2.01	0.25	83% (0%, NC)	10.59 (0, NC)	NC
Bone-borne	Pst-Exp	Inclination 1 <sup>st</sup> molar (right)	2	-1.47	-3.90, 0.95	0.23	0% (0%, 98%)	0 (0, 189.07)	NC
Bone-borne	Pst-Exp	Inclination 1 <sup>st</sup> premolar (left)	2	-2.49	-5.19, 0.22	0.07	60% (0%, 100%)	2.31 (0, 483.98)	NC
Bone-borne	Pst-Exp	Inclination 1 <sup>st</sup> premolar (right)	2	-4.05	-5.97, -2.13	<0.001	0% (0%, 98%)	0 (0, 93.81)	NC
Bone-borne	Reten	Intermolar width (crown)	3	0.15	-0.27, 0.56	0.49	0% (0%, 88%)	0 (0, 1.23)	-2.54, 2.83
Bone-borne	Reten	Inter-1 <sup>st</sup> -premolar width (crown)	3	-0.66	-1.90, 0.58	0.30	77% (0%, 99%)	0.88 (0, 22.64)	-15.06, 13.74
Bone-borne	Reten	Inclination 1 <sup>st</sup> molar (left)	2	-1.89	-9.48, 5.70	0.63	87% (10%, NC)	26.04 (0.45, NC)	NC
Bone-borne	Reten	Inclination 1 <sup>st</sup> molar (right)	2	-0.20	-3.91, 3.51	0.92	59% (0%, 100%)	4.33 (0, 913.80)	NC
Bone-borne	Reten	Inclination 1 <sup>st</sup> premolar (left)	2	-2.38	-9.53, 4.76	0.51	90% (31%, NC)	23.94 (1.24, NC)	NC
Bone-borne	Reten	Inclination 1 <sup>st</sup> premolar (right)	2	-0.77	-3.02, 1.48	0.50	0% (0%, 98%)	0 (0, 154.35)	NC
Bone-borne	Reten	Nasal cavity width	2	*0.41	*-0.03, 0.84	0.07	0% (0%, 99%)	0 (0, 7.60)	NC
Hybrid	Reten	Inter canine width (crown)	2	-0.22	-0.98, 0.55	0.58	36% (0%, 100%)	0.16 (0, 55.23)	NC
Hybrid	Reten	Intermolar width (crown)	2	0.18	-0.40, 0.76	0.55	0% (0%, 98%)	0 (0, 28.03)	NC
Hybrid	Reten	Inter-1 <sup>st</sup> -premolar width (crown)	2	-1.96	-6.18, 2.27	0.36	89% (27%, NC)	8.36 (0.38, NC)	NC
Hybrid	Reten	Inclination 1 <sup>st</sup> molar (left)	2	-1.29	-3.61, 1.03	0.28	0% (0%, 99%)	0 (0, 341.30)	NC
Hybrid	Reten	Inclination 1 <sup>st</sup> molar (right)	2	-1.12	-6.96, 4.72	0.71	66% (0%, NC)	11.75 (0, NC)	NC
Hybrid	Reten	Inclination 1 <sup>st</sup> premolar (left)	2	-3.97	-7.08, -0.86	0.01	49% (0%, 100%)	2.70 (0, 685.54)	NC
Hybrid	Reten	Inclination 1 <sup>st</sup> premolar (right)	2	-0.79	-3.18, 1.60	0.52	0% (0%, 98%)	0 (0, 181.80)	NC

CI, confidence interval; MD, mean difference; NC, non-calculable; PrI, predictive interval; Pst-Exp, post expansion; Reten, post retention period (at least 3 months).

\* pertains to standardized mean difference, as two similar outcomes were pooled together: nasal cavity width at orbita and nasal cavity width at the 1<sup>st</sup> premolar.

**Table 3a.** Summary of findings table according to the GRADE approach for the comparison of bone-borne versus tooth-borne rapid maxillary expansion.

<b>Outcome</b> Trials (patients)	<b>Anticipated absolute effects<sup>a</sup> (95% CI)</b>			<b>Quality of the evidence (GRADE)<sup>c</sup></b>	<b>What happens</b>
	<b>Tooth-borne RME</b>	<b>Bone-borne RME</b>	<b>Difference</b>		
Suture opening at 1 <sup>st</sup> premolar Post-retention 40 patients (1 trial)	1.3 mm	-	2.3 mm more (1.7 to 2.9 more)	⊕⊕⊕○ moderate <sup>d</sup> due to imprecision	Probably greater sutural opening with bone-borne RME
Suture opening at 1 <sup>st</sup> molar Post-retention 40 patients (1 trial)	1.1 mm	-	2.0 mm more (1.4 to 2.6 more)	⊕⊕⊕○ moderate <sup>d</sup> due to imprecision	Probably greater sutural opening with bone-borne RME
Buccal tipping of 1 <sup>st</sup> premolar Post-retention 73 patients (2 trials)	3.9°	-	2.4° less (9.5 less to 4.8 more)	⊕○○○ very low <sup>d,e,f</sup> due to bias, inconsistency, imprecision	Little to no difference in premolar buccal tipping
Buccal tipping of 1 <sup>st</sup> molar Post-retention 73 patients (2 trials)	5.7°	-	1.9° less (9.5 less to 5.7 more)	⊕○○○ very low <sup>d,e,f</sup> due to bias, inconsistency, imprecision	Little to no difference in molar buccal tipping
Nasal cavity width at 1 <sup>st</sup> premolar/orbita <sup>§</sup> Post-retention 81 patients (2 trials)	1.8 mm <sup>§</sup>	-	0.7 mm more (0.1 less to 1.4 more)	⊕⊕○○ low <sup>d,e</sup> due to bias, imprecision	Little to no difference in nasal cavity width
Root resorption volume at 1 <sup>st</sup> molar Post-retention 41 patients (1 trial)	49.3 mm <sup>3</sup>	-	17.8 mm <sup>3</sup> less (46.0 to 10.4 more)	⊕⊕○○ low <sup>d,e</sup> due to bias, imprecision	Little to no difference in root resorption volume

Bone-borne versus tooth-borne rapid maxillary expansion.

Population & intervention: adolescent or adult patients with skeletal maxillary deficit.

Settings: university clinics, private practices, and clinics (Canada, Netherlands, Sweden, Turkey,).

<sup>a</sup> The basis for the risk in the control group (e.g., the median control group risk across studies) is provided in footnotes. The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

<sup>b</sup> Response in the control group is based on average response of included trials.

<sup>c</sup> Starts from "high", due to the inclusion of randomized studies.

<sup>d</sup> Downgraded by one point due to imprecision, as the optimal information size was judged not to be met.

<sup>e</sup> Downgraded by one point for risk of bias (lack of blind outcome assessment).

<sup>f</sup> Downgraded one for inconsistency ( $I^2 > 75\%$ ).

CI, confidence interval; GRADE, Grading of Recommendations Assessment, Development and Evaluation.

<sup>§</sup>Standardized mean difference was used for the meta-analysis and was back-translated to natural units based on the data from the Celenk-Koca 2018 trial.

**Table 3b.** Summary of findings table according to the GRADE approach for the comparison of hybrid (tooth-bone-borne) versus tooth-borne rapid maxillary expansion.

Outcome Trials (patients)	Relative effect (95% CI)	Anticipated absolute effects <sup>a</sup> (95% CI)			Quality of the evidence (GRADE) <sup>c</sup>	What happens
		Tooth-borne RME	Hybrid (tooth-bone-borne) RME	Difference		
External maxillary width at 1 <sup>st</sup> molar Post-retention 25 patients (1 trial)	-	2.0 mm	-	0.6 mm more (1.4 less to 2.7 more)	⊕○○○ low <sup>d,e</sup> due to bias, imprecision	Little to no difference in external maxillary width at 1 <sup>st</sup> molars
Buccal tipping of 1 <sup>st</sup> premolar Post-retention 56 patients (2 trials)	-	3.7°	-	4.0° less (0.9 to 7.1 less)	⊕⊕○○ moderate <sup>e,f</sup> due to bias, imprecision	Probably less premolar tipping with hybrid RME
Buccal tipping of 1 <sup>st</sup> molar Post-retention 56 patients (2 trials)	-	4.3°	-	1.3° less (3.6 less to 1.0 more)	⊕⊕○○ moderate <sup>e,f</sup> due to bias, imprecision	Little to no difference in molar buccal tipping
Nasal resistance Post-expansion 30 patients (1 trial)	-	0.9 Pa s/cm <sup>3</sup>	-	0.2 Pa s/cm <sup>3</sup> less (0 to 0.4 less)	⊕⊕⊕○ moderate <sup>e</sup> due to imprecision	Probably lower nasal resistance with hybrid RME
Analgesic use on 1 <sup>st</sup> expansion day Post-retention 50 patients (1 trial)	RR 0.8 (0.3 to 1.8)	36.0%	28.1% (12.2% to 63.4%)	7.9% less (13.8% less to 27.4% more)	⊕⊕⊕○ moderate <sup>e</sup> due to imprecision	Little to no difference in analgesic use

Bone-borne versus tooth-borne rapid maxillary expansion.

Population & intervention: adolescent or adult patients with skeletal maxillary deficit.

Settings: university clinics, private practices, and clinics (Canada, Netherlands, Sweden, Turkey,).

<sup>a</sup> The basis for the risk in the control group (e.g., the median control group risk across studies) is provided in footnotes. The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

<sup>b</sup> Response in the control group is based on average response of included trials.

<sup>c</sup> Starts from "high", due to the inclusion of randomized studies.

<sup>d</sup> Downgraded by two points due to risk of bias (potentially inadequate randomization and lack of blind outcome assessment).

<sup>e</sup> Downgraded by one point due to imprecision, as the optimal information size was judged not to be met.

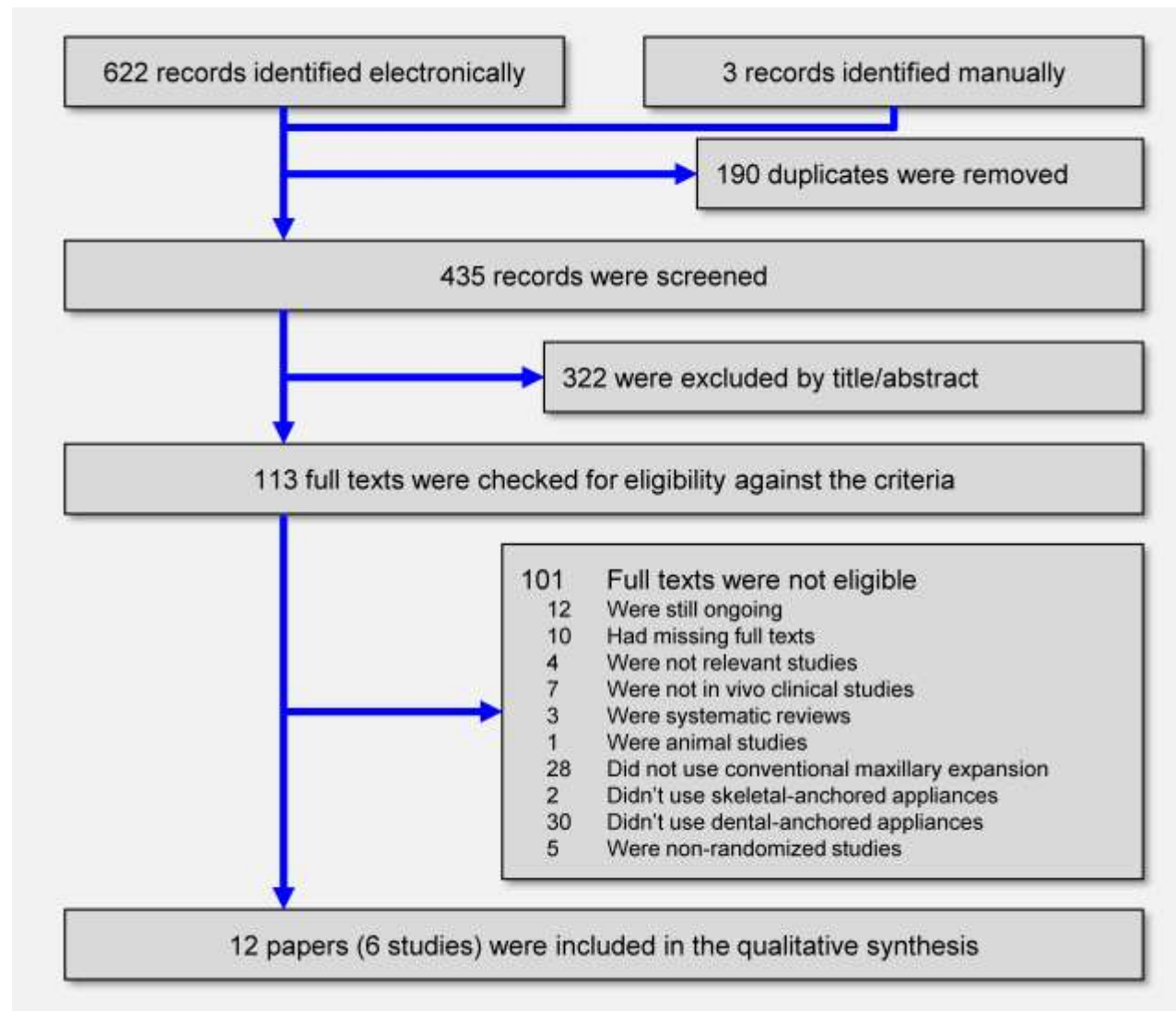
<sup>f</sup> Downgraded by one point for risk of bias (lack of blind outcome assessment).

<sup>f</sup> Downgraded one for inconsistency ( $I^2 > 75\%$ ).

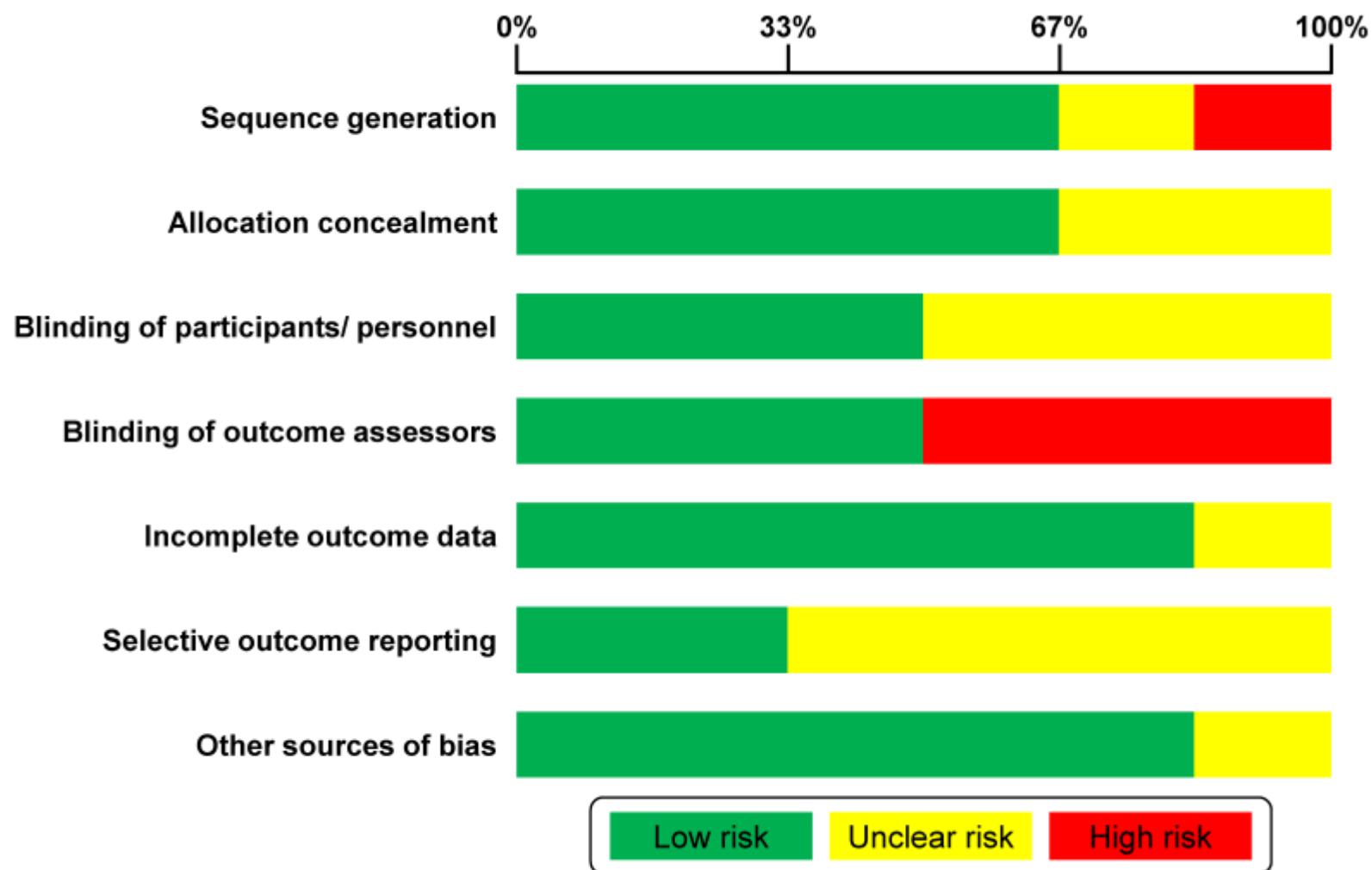
CI, confidence interval; GRADE, Grading of Recommendations Assessment, Development and Evaluation.

## Figure Legends

**Figure 1.** PRISMA flowdiagram for identification and selection of eligible trials.



**Figure 2.** Risk of bias summary for included randomized trials with the Cochrane tool.



**Appendix 1.** Literature searched conducted to identify eligible studies (last search date September 28<sup>th</sup>, 2018).

Search for clinical studies				Search for randomized studies			
Database	Search	Limits	Hits	Database	Search	Hits	
MEDLINE (via PubMed)	("maxillary expansion" OR ((expand* OR expans*) AND maxill*)) AND ("bone-anchorage" OR "bone-anchored" OR "bone-borne" OR "implant-anchorage" OR "implant-anchored" OR "implant-borne" OR "mini-implant" OR "minipin" OR "mini-pin" OR "miniscrew" OR "mini-screw" OR "mini-implant" OR "palatal implant" OR "skeletal anchorage" OR "skeletally-anchored" OR "transpalatal distraction")	Humans	177	MEDLINE (via PubMed)	("maxillary expansion" OR ((expand* OR expans*) AND maxill*)) AND ("bone-anchorage" OR "bone-anchored" OR "bone-borne" OR "implant-anchorage" OR "implant-anchored" OR "implant-borne" OR "mini-implant" OR "minipin" OR "mini-pin" OR "miniscrew" OR "mini-screw" OR "mini-implant" OR "palatal implant" OR "skeletal anchorage" OR "skeletally-anchored" OR "transpalatal distraction") AND (randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR clinical trials as topic[mesh:noexp] OR randomly[tiab] OR trial[ti] NOT (animals[mh] NOT humans [mh]))	26	
Embase	Same as MEDLINE	Human	30	Embase	("maxillary expansion" OR ((expand* OR expans*) AND maxill*)) AND ("bone-anchorage" OR "bone-anchored" OR "bone-borne" OR "implant-anchorage" OR "implant-anchored" OR "implant-borne" OR "mini-implant" OR "minipin" OR "mini-pin" OR "miniscrew" OR "mini-screw" OR "mini-implant" OR "palatal implant" OR "skeletal anchorage" OR "skeletally-anchored" OR "transpalatal distraction") AND ('crossover procedure':de OR 'double-blind procedure':de OR 'randomized controlled trial':de OR 'single-blind procedure':de OR random*:de,ab,ti OR factorial*:de,ab,ti OR crossover*:de,ab,ti OR ((cross NEXT/1 over*):de,ab,ti) OR placebo*:de,ab,ti OR ((doubl* NEAR/1 blind*):de,ab,ti) OR ((singl* NEAR/1 blind*):de,ab,ti) OR assign*:de,ab,ti OR allocat*:de,ab,ti OR volunteer*:de,ab,ti) AND [embase]/lim	8	
CDSR	Same as MEDLINE		0	CDSR	("maxillary expansion" OR ((expand* OR expans*) AND maxill*)) AND ("bone-anchorage" OR "bone-anchored" OR "bone-borne" OR "implant-anchorage" OR "implant-anchored" OR "implant-borne" OR "mini-implant" OR "minipin" OR "mini-pin" OR "miniscrew" OR "mini-screw" OR "mini-implant" OR "palatal implant" OR "skeletal anchorage" OR "skeletally-anchored" OR "transpalatal distraction")	0	
DARE	Same as MEDLINE		0	DARE	Same as CDSR	0	
CENTRAL	Same as MEDLINE		30	CENTRAL	Same as CDSR	31	
Scopus	( TITLE-ABS-KEY ( ( "maxillary expansion" OR ( ( expand* OR expans* ) AND maxill* ) ) ) AND TITLE-ABS-KEY ( ( "bone-anchorage" OR "bone-anchored" OR "bone-borne" OR "implant-anchorage" OR "implant-anchored" OR "implant-borne" OR "mini-implant" OR "minipin" OR "mini-pin" OR "miniscrew" OR "mini-screw" OR "mini-implant" OR "palatal implant" OR "skeletal anchorage" OR "skeletally-anchored" OR "transpalatal distraction" ) ) )	Dentistry Human/humans	131	Scopus	#1: ( INDEXTERMS ( "clinical trials" OR "clinical trials as a topic" OR "randomized controlled trial" OR "Randomized Controlled Trials as Topic" OR "controlled clinical trial" OR "Controlled Clinical Trials" OR "random allocation" OR "Double-Blind Method" OR "Single-Blind Method" OR "Cross-Over Studies" OR "Placebos" OR "multicenter study" OR "double blind procedure" OR "single blind procedure" OR "crossover procedure" OR "clinical trial" OR "controlled study" OR "randomization" OR "placebo" ) ) OR ( TITLE-ABS-KEY ( ( "clinical trials" OR "clinical trials as a topic" OR "randomized controlled trial" OR "Randomized Controlled Trials as Topic" OR "controlled clinical trial" OR "Controlled Clinical Trials as Topic" OR "random allocation" OR "randomly allocated" OR "allocated randomly" OR "Double-Blind Method" OR "Single-Blind Method" OR "Cross-Over Studies" OR "Placebos" OR "cross-over trial" OR "single blind" OR "double blind" OR "factorial design" OR "factorial trial" ) ) ) OR ( TITLE-ABS ( clinical trial" OR trial" OR rct" OR random* OR blind* ) ) )		
					#2: ("maxillary expansion" OR ((expand* OR expans*) AND maxill*)) AND ("bone-anchorage" OR "bone-anchored" OR "bone-borne" OR "implant-anchorage" OR "implant-anchored" OR "implant-borne" OR "mini-implant" OR "minipin" OR "mini-pin" OR "miniscrew" OR "mini-screw" OR "mini-implant" OR "palatal implant" OR "skeletal anchorage" OR "skeletally-anchored" OR "transpalatal distraction")		
					#1 AND #2	46	
Web of Knowledge	Same as MEDLINE	DENTISTRY ORAL SURGERY MEDICINE	205	Web of Knowledge	#1: TS= clinical trial" OR TS=research design OR TS=comparative stud* OR TS=evaluation stud* OR TS=controlled trial* OR TS=follow-up stud* OR TS=prospective stud* OR TS=random* OR TS=placebo* OR TS=(single blind*) OR TS=(double blind*)		
					#2: ("maxillary expansion" OR ((expand* OR expans*) AND maxill*)) AND ("bone-anchorage" OR "bone-anchored" OR "bone-borne" OR "implant-anchorage" OR "implant-anchored" OR "implant-borne" OR "mini-implant" OR "minipin" OR "mini-pin" OR "miniscrew" OR "mini-screw" OR "mini-implant" OR "palatal implant" OR "skeletal anchorage" OR "skeletally-anchored" OR "transpalatal distraction")	79	
Virtual Health Library	Same as MEDLINE		19	Virtual Health Library	("maxillary expansion" OR ((expand* OR expans*) AND maxill*)) AND ("bone-anchorage" OR "bone-anchored" OR "bone-borne" OR "implant-anchorage" OR "implant-anchored" OR "implant-borne" OR "mini-implant" OR "minipin" OR "mini-pin" OR "miniscrew" OR "mini-screw" OR "mini-implant" OR "palatal implant" OR "skeletal anchorage" OR "skeletally-anchored" OR "transpalatal distraction") AND random*	0	
ClinicalTrials.gov	("maxillary expansion" OR ((expand* OR expans*) AND maxill*))		17	ClinicalTrials.gov	("maxillary expansion" OR ((expand* OR expans*) AND maxill*))	17	
<b>SUM (with overlap)</b>			<b>432</b>	<b>SUM (with overlap)</b>			<b>207</b>

CDSR, Cochrane Database of Systematic Reviews; CENTRAL, Cochrane Central Register of Controlled Trials; DARE, Database of Abstracts of Reviews of Effects.

## **Appendix 2.** Additional information about this review, including deviations from protocol.

### Deviations from protocol

- We decided post hoc to use the standardized mean difference to combine to similar measurements of the nasal cavity width (at the premolars and at the orbita). This is reported as a post hoc decision.
- The number needed to treat was planned to be calculated to clinically translate statistically significant relative risk, but no statistically significant relative risks were ultimately found.
- We had initially planned to use the Paule-Mandel variance estimator for the random-effect model instead of the DerSimonian-Laird one, according to appropriate guidance at the time of protocol writing. However, more recent guidance (from the same group of the first guidance) subsequently suggested a REML approach as a more appropriate and therefore this was ultimately chosen.
- Possible sources of heterogeneity were planned a priori in the protocol to be sought through mixed-effects subgroup analyses and random-effects meta-regression for meta-analyses of at least five studies. This could ultimately not be assessed, as less than 5 studies were included in any meta-analysis.
- Reporting biases were planned to be assessed for meta-analyses of at least 10 studies using contour-enhanced funnel plots and with the Egger's weighted regression test. This could ultimately not be assessed, as less than 10 studies were included in any meta-analysis.
- The robustness of the results was planned to be checked a priori with sensitivity analyses based on (i) inclusion/exclusion of trials with low risk of bias and (ii) improvement of the GRADE classification. However, all results were based on one, two, or seldom three trials and therefore any trial omissions were not deemed stable.

### Appendix 3. List of studies identified from the literature and their inclusion/exclusion status, with reasons.

Nr	Paper	Status
Exclusion by title / abstract		
1	{NCT00519415}. Comparative Results of Maxillary Deficiency Treatment by Tongue Plate and Facemask in Growing Patients. Completed	Excluded by title
2	{NCT01770782}. Orthodontic Retention on the Maxillary Stability After SARME Using Laser Scanner. Completed	Excluded by title
3	{NCT02179593}. Effectiveness of SARPE With 3 and 2-Segment Technique: A Randomized Clinical Trial. Active, not recruiting	Excluded by title
4	{NCT02574117}. Cone Beam Computed Tomography for Evaluating Corticotomy-assisted Maxillary Expansion. Completed	Excluded by title
5	{NCT03267927}. Management of Obstructive Sleep Apnea (OSA) in Children and Maxillary and Mandibular Development. Recruiting	Excluded by title
6	Adolphs N, Ernst N, Menneking H, Hoffmeister B. Transpalatal distraction--state of the art for the individual management of transverse maxillary deficiency--a review of 50 consecutive cases. J Craniomaxillofac Surg. 2014;42(8):1669-74.	Excluded by title
7	Aglarci C, Esenlik E, Findik Y. Comparison of short-term effects between face mask and skeletal anchorage therapy with intermaxillary elastics in patients with maxillary retrognathia. Eur J Orthod 2016;38(3):313-23.	Excluded by title
8	Akay MC, Aras I, Gunbay T, Aras A. Does transpalatal distraction affect pharyngeal airway dimensions and related soft tissues? J Oral Maxillofac Surg. 2014;72(8):1559-64.	Excluded by title
9	Akay MC. IS THE MIDLINE BUCCAL INCISION IMPORTANT FOR THE OUTCOME OF SURGICALLY ASSISTED RAPID MAXILLARY EXPANSION? In reply. Journal of Oral and Maxillofacial Surgery. 2010;68(11):2924-.	Excluded by title
10	Akis H, Doruk C. Dentofacial Effects of Fixed Functional Appliances with or without Mini Screw Anchorage in the Treatment of Class II Division I Malocclusion: A Finite Element Analysis. Turkish Journal of Orthodontics. 2018;31(1):7-12.	Excluded by title
11	Alyessary AS, Yap AU, Othman SA, Rahman MT, Al-Namnam NM, Radzi Z. Is there an optimal initial amount of activation for midpalatal suture expansion? : A histomorphometric and immunohistochemical study in a rabbit model. J Orofac Orthop. 2018;79(3):169-79.	Excluded by title
12	Alyessary AS, Yap AUJ, Othman SA, Ibrahim N, Rahman MT, Radzi Z. Bone-borne accelerated sutural expansion: A microcomputed tomography study in rabbits. American Journal of Orthodontics and Dentofacial Orthopedics. 2018;154(2):260-9.	Excluded by title
13	Alyessary AS, Yap AUJ, Othman SA, Rahman MT, Radzi Z. Effect of Piezoelectric Sutural Osteotomies on Accelerated Bone-Borne Sutural Expansion. J Oral Maxillofac Surg. 2018;76(3):616-30.	Excluded by title
14	Alyessary AS, Yap AUJ, Othman SA, Rahman MT, Radzi Z. Effect of Piezoelectric Sutural Osteotomies on Accelerated Bone-Borne Sutural Expansion. Journal of Oral and Maxillofacial Surgery. 2017.	Excluded by title
15	Angelieri F, Ruellas AC, Yatabe MS, Cevitanes LHS, Franchi L, Toyama-Hino C, et al. Zygomaticomaxillary suture maturation: Part IIThe influence of sutural maturation on the response to maxillary protraction. Orthodontics & Craniofacial Research. 2017;20(3):152-63.	Excluded by title
16	Asscherickx K, Govaerts E, Aerts J, Vande Vannet B. Maxillary changes with bone-borne surgically assisted rapid palatal expansion: A prospective study. Am J Orthod Dentofacial Orthop. 2016;149(3):374-83.	Excluded by title
17	Aziz SR, Tanchyk A. Surgically assisted palatal expansion with a bone-borne self-retaining palatal expander. J Oral Maxillofac Surg. 2008;66(9):1788-93.	Excluded by title
18	Baccetti T, Clerck HJ, Cevitanes LH, Franchi L. Morphometric analysis of treatment effects of bone-anchored maxillary protraction in growing Class III patients. Eur J Orthod 2011;33(2):121-5.	Excluded by title
19	Baek SH, Kim KW, Choi JY. New treatment modality for maxillary hypoplasia in cleft patients Protraction facemask with miniplate anchorage. Angle Orthod 2010;80(4):783-91.	Excluded by title
20	Baek SH, Park YH, Chung JH, Kim S, Choi JY. Orthodontic and orthopedic treatment for a growing patient with Tessier number 0 cleft. Korean Journal of Orthodontics. 2018;48(2):113-24.	Excluded by title
21	Baek SH, Seo YJ. Application of orthodontic mini-implants and ligation for absolute skeletal anchorage to the intraoral labiolingual appliance: midface distraction osteogenesis cases treated with the RED System. J Craniofac Surg. 2011;22(2):609-13.	Excluded by title
22	Baik UB, Chun YS, Jung MH, Sugawara J. Protraction of mandibular second and third molars into missing first molar spaces for a patient with an anterior open bite and anterior spacing. Am J Orthod Dentofacial Orthop 2012;141(6):783-95.	Excluded by title
23	Batra P, Agrawal V, Kiran HJ, Madanagowda SB. Treatment of a patient with a bilateral cleft lip and palate with implants and surgery of the maxillary anterior region. World J Orthod. 2010;11(4):380-6.	Excluded by title
24	Battistetti GD, Sinaglia AC, Fleig CdN, Bombonatti R. Nova proposta de expansor maxilar com ancoragem óssea: relato de caso clínico. Rev Clin Ortod Dent Press. 2011;10(1):28-34.	Excluded by title
25	Bicalho RdF, Bicalho JS, Laboissiere Jr M. Utilização de microparafuso ortodôntico autoperfurante para reabilitação temporária de incisivo lateral superior. ImplantNews. 2010;7(3):389-96.	Excluded by title
26	Bila M, Defranco J, Nadjimi N, Renier L, Stevens S, Vanassche B, et al. CBCT analysis of skeletal, dental and nasal changes after transpalatal distraction. International Journal of Oral and Maxillofacial Surgery. 2015;44:e39.	Excluded by title
27	Block MS, Akin R, Chang A, Gottsegen GB, Gardiner D. Skeletal and dental movements after anterior maxillary advancement using implant-supported distraction osteogenesis in dogs. Journal of Oral and Maxillofacial Surgery. 1997;55(12):1433-9.	Excluded by title
28	Bozkaya E, Yuksel AS, Bozkaya S. Zygomatic miniplates for skeletal anchorage in orthopedic correction of Class 111 malocclusion: A controlled clinical trial. Korean J Orthod 2017;47(2):118-29.	Excluded by title
29	Buzatta LN, Toyofuku ACCM, Pinto AdS, Gandini Junior LG, Shimizu RH. Expansão rápida da maxila osseossuportada: um relato de caso e passo a passo laboratorial. Ortho Sci, Orthod sci pract. 2017;10(39):223-33.	Excluded by title
30	Byloff FK, Mossaz CF. Skeletal and dental changes following surgically assisted rapid palatal expansion. Eur J Orthod 2004;26(4):403-9.	Excluded by title
31	Cai M, Shen GF. [Development of bone-anchored surgically assisted rapid maxillary expansion]. Shanghai Kou Qiang Yi Xue. 2009;18(4):441-5.	Excluded by title
32	Camps-Pereperez I, Guijarro-Martinez R, Peiro-Guijarro MA, Hernandez-Alfaro F. The value of cone beam computed tomography imaging in surgically assisted rapid palatal expansion: a systematic review of the literature. International Journal of Oral and Maxillofacial Surgery. 2017;46(7):827-38.	Excluded by title
33	Carlino F, Cortese A. Original technique for mandibular transversal surgical expansion via a tooth-borne lingual device. International Journal of Oral and Maxillofacial Surgery. 2015;44:e49.	Excluded by title
34	Carlino F, Pantaleo G, Ciuffolo F, Claudio PP, Cortese A. New Technique for Mandibular Symphyseal Distraction by a Double-Level Anchorage and Fixation System: Advantages and Results. J Craniofac Surg. 2016;27(6):1469-75.	Excluded by title
35	Carneiro JT, Jr., Paschoal EH, Carreira AS, Real RP. Carotid cavernous fistula after surgically assisted rapid maxillary expansion with a bone anchored appliance. Int J Oral Maxillofac Surg. 2013;42(3):326-8.	Excluded by title
36	Carpentier S, van Gastel J, Schoenaers J, Carels C, Vander Poorten V, Coucke W, et al. Evaluation of Transverse Maxillary Expansion After a Segmental Posterior Subapical Maxillary Osteotomy in Cleft Lip and Palate Patients With Severe Collapse of the Lateral Maxillary Segments. Cleft Palate-Craniofacial Journal. 2014;51(6):651-7.	Excluded by title
37	Carvalho Trojan L, Andres Gonzalez-Torres L, Claudia Moreira Melo A, Barbosa de Las Casas E. Stresses and Strains Analysis Using Different Palatal Expander Appliances in Upper Jaw and Midpalatal Suture. Artif Organs. 2017;41(6):E41-e51.	Excluded by title
38	Cevitanes L, Baccetti T, Franchi L, McNamara JA, Jr., De Clerck H. Comparison of two protocols for maxillary protraction: bone anchors versus face mask with rapid maxillary expansion. Angle Orthod. 2010;80(5):799-806.	Excluded by title
39	Cha BK, Choi DS, Ngan P, Jost-Brinkmann PG, Kim SM, Jang IS. Maxillary protraction with miniplates providing skeletal anchorage in a growing Class III patient. Am J Orthod Dentofacial Orthop. 2011;139(1):99-112.	Excluded by title
40	Choi SH, Kang DY, Hwang CJ. Adult patient with hemifacial microsomia treated with combined orthodontics and distraction osteogenesis. Am J Orthod Dentofacial Orthop. 2014;145(1):72-84.	Excluded by title
41	Cortese A, de Cristofaro M, Savastano G. A new transpalatal distraction device: Report of three cases with surgical and occlusal evaluations. Proceedings of the 7th European Craniofacial Congress2003. p. 57-67.	Excluded by title
42	Cortese A, Savastano G, Savastano M, Spagnuolo G, Papa F. New Technique: Le Fort I Osteotomy for Maxillary Advancement and Palatal Distraction in 1 Stage. Journal of Oral and Maxillofacial Surgery. 2009;67(1):223-8.	Excluded by title



43	Cousley RR. A clinical strategy for maxillary molar intrusion using orthodontic mini-implants and a customized palatal arch. J Orthod. 2010;37(3):202-8.	Excluded by title
44	Cousley RR. Molar intrusion in the management of anterior openbite and 'high angle' Class II malocclusions. J Orthod. 2014;41 Suppl 1:S39-46.	Excluded by title
45	Cousley RRJ. Molar intrusion in the management of anterior openbite and 'high angle' Class II malocclusions. Journal of Orthodontics. 2014;41:S39-S46.	Excluded by title
46	Cunha ACD, Lee H, Nojima LI, Nojima M, Lee KJ. Miniscrew-assisted rapid palatal expansion for managing arch perimeter in an adult patient. Dental Press J Orthod. 2017;22(3):97-108.	Excluded by title
47	De Clerck EEB, Swennen GRJ. Success rate of miniplate anchorage for bone anchored maxillary protraction. Angle Orthod. 2011;81(6):1010-3.	Excluded by title
48	De Clerck H, Nguyen T, de Paula LK, Cevidanes L. Three-dimensional assessment of mandibular and glenoid fossa changes after bone-anchored Class III intermaxillary traction. Am J Orthod Dentofacial Orthop. 2012;142(1):25-31.	Excluded by title
49	de Gijt JP, Gul A, Sutedja H, Wolvius EB, van der Wal KG, Koudstaal MJ. Long-term (6.5 years) follow-up of mandibular midline distraction. J Craniomaxillofac Surg. 2016;44(10):1576-82.	Excluded by title
50	de Gijt JP, Gul A, Tjoa STH, Wolvius EB, van der Wal KGH, Koudstaal MJ. Follow up of surgically-assisted rapid maxillary expansion after 6.5 years: skeletal and dental effects. British Journal of Oral & Maxillofacial Surgery. 2017;55(1):56-60.	Excluded by title
51	de Menezes LM, de Oliveira RB, Weissheimer A, Avelar RL. Midfacial Protraction With Skeletal Anchorage After Pterygomaxillary Separation. J Craniofac Surg. 2016;27(6):1561-4.	Excluded by title
52	Deeb W, Hansen L, Hotan T, Hietschold V, Harzer W, Tausche E. Changes in nasal volume after surgically assisted bone-borne rapid maxillary expansion. Am J Orthod Dentofacial Orthop. 2010;137(6):782-9.	Excluded by title
53	Defrancoq E, Weckx K, Nadimi N, Van HG, Vercruyse H, Van Der Dussen N, et al. Cone Beam CT assessment of nasal septal deviation changes following surgical rapid maxillary expansion. Xx Congress of the European Association of Cranio-Maxillo-Facial-Surgery. 2010:101-12.	Excluded by title
54	Di Leonardo B, Ludwig B, Lissan JA, Contardo L, Mura R, Hourfar J. Insertion torque values and success rates for paramedian insertion of orthodontic mini-implants. Journal of Orofacial Orthopedics-Fortschritte Der Kieferorthopadie. 2018;79(2):109-15.	Excluded by title
55	Eid OM, Ramadan AAF, Nadim MA, Hamed TAB. Maxillary protraction using orthodontic miniplates in correction of Class III malocclusion during growth. Journal of the World Federation of Orthodontists. 2016;5(3):100-6.	Excluded by title
56	Elnagar MH, Elshourbagy E, Ghabashy S, Khedr M, Evans CA. Comparative evaluation of 2 skeletally anchored maxillary protraction protocols. Am J Orthod Dentofacial Orthop. 2016;150(5):751-62.	Excluded by title
57	Elnagar MH, Elshourbagy E, Ghabashy S, Khedr M, Evans CA. Dentoalveolar and arch dimension changes in patients treated with miniplate-anchored maxillary protraction. Am J Orthod Dentofacial Orthop. 2017;151(6):1092-106.	Excluded by title
58	Elnagar MH, Elshourbagy E, Ghabashy S, Khedr M, Kusnoto B, Evans CA. Three-dimensional assessment of soft tissue changes associated with bone-anchored maxillary protraction protocols. Am J Orthod Dentofacial Orthop. 2017;152(3):336-47.	Excluded by title
59	El-Sayed KM, Khalil H. Transpalatal distraction osteogenesis prior to alveolar bone grafting in cleft lip and palate patients. Int J Oral Maxillofac Surg. 2010;39(8):761-6.	Excluded by title
60	El-Sayed KM, Khalil H. Transpalatal distraction osteogenesis prior to alveolar bone grafting in cleft lip and palate patients. International Journal of Oral and Maxillofacial Surgery. 2010;39(8):761-6.	Excluded by title
61	Evans CA, Scarfe WC, Ahmad M, Cevidanes LHS, Ludlow JB, Palomo JM, et al. Clinical recommendations regarding use of cone beam computed tomography in orthodontics. Position statement by the American Academy of Oral and Maxillofacial Radiology. Oral Surgery Oral Medicine Oral Pathology Oral Radiology. 2013;116(2):238-57.	Excluded by title
62	Feng XX, Li JH, Li Y, Zhao ZH, Zhao S, Wang J. Effectiveness of TAD-anchored maxillary protraction in late mixed dentition A systematic review. Angle Orthod. 2012;82(6):1107-14.	Excluded by title
63	Finn MD. Surgical Assistance for Rapid Orthodontic Treatment and Temporary Skeletal Anchorage. Oral and Maxillofacial Surgery Clinics of North America. 2014;26(4):539-+.	Excluded by title
64	Finn MD. Surgical assistance for rapid orthodontic treatment and temporary skeletal anchorage. Oral Maxillofac Surg Clin North Am. 2014;26(4):539-50.	Excluded by title
65	Fukui T, Fukui K, Yoshida K, Tsuruta M, Galang-Boquiren MTS. Invisible treatment of a severe Class II deep over bite with narrow mandibular dental arch with multilingual bracket appliances. Journal of the World Federation of Orthodontists. 2017;6(2):69-79.	Excluded by title
66	Gamez SN, Goss AN. Surgically-assisted rapid maxillary expansion of narrowed maxillae: a case-cohort study. Australian Orthodontic Journal. 2013;29(1):21-7.	Excluded by title
67	Gamble J, Lagravere MO, Major PW, Heo G. New statistical method to analyze three-dimensional landmark configurations obtained with cone-beam CT: basic features and clinical application for rapid maxillary expansion. Korean J Radiol. 2012;13(2):126-35.	Excluded by title
68	Gamble J, Lagravere MO, Major PW, Heo G. New statistical method to analyze three-dimensional landmark configurations obtained with cone-beam CT: Basic features and clinical application for rapid maxillary expansion. Korean Journal of Radiology. 2012;13(2):126-35.	Excluded by title
69	Garib D, Yatabe M, de Souza Faco RA, Gregorio L, Cevidanes L, de Clerck H. Bone-anchored maxillary protraction in a patient with complete cleft lip and palate: A case report. Am J Orthod Dentofacial Orthop. 2018;153(2):290-7.	Excluded by title
70	Garreau E, Bouscaillou J, Rattier S, Ferri J, Raoul G. Bone-borne distractor versus tooth-borne distractor for orthodontic distraction after surgical maxillary expansion: The patient's point of view. Int Orthod. 2016;14(2):214-32.	Excluded by title
71	Garreau E, Wojcik T, Rakotomalala H, Raoul G, Ferri J. Symphyseal distraction in the context of orthodontic treatment: A series of 35 cases. International Orthodontics. 2015;13(1):81-95.	Excluded by title
72	Gautam P, Zhao LP, Patel P. Determining the osteotomy pattern in surgically assisted rapid maxillary expansion in a unilateral palatal cleft A finite element model approach. Angle Orthod. 2011;81(3):410-9.	Excluded by title
73	Ge YS, Liu J, Chen L, Han JL, Guo X. Dentofacial effects of two facemask therapies for maxillary protraction Miniscrew implants versus rapid maxillary expanders. Angle Orthodontist. 2012;82(6):1083-91.	Excluded by title
74	Ge YS, Liu J, Chen L, Han JL, Guo X. Dentofacial effects of two facemask therapies for maxillary protraction. Angle Orthod. 2012;82(6):1083-91.	Excluded by title
75	Gerlach KL, Zahl C. Surgically assisted rapid palatal expansion using a new distraction device: Report of a case with an epimucosal fixation. Journal of Oral and Maxillofacial Surgery. 2005;63(5):711-3.	Excluded by title
76	Goonewardene M, Allan B. Biomechanics and Treatment of Dentofacial Deformity. Biomechanical Foundation of Clinical Orthodontics 2015. p. 389-432.	Excluded by title
77	Gunbay T, Akay MC, Aras A, Gomel M. Effects of transmandibular symphyseal distraction on teeth, bone, and temporomandibular joint. J Oral Maxillofac Surg. 2009;67(10):2254-65.	Excluded by title
78	Gunbay T, Akay MC, Aras A, Gomel M. Effects of Transmandibular Symphyseal Distraction on Teeth, Bone, and Temporomandibular Joint. Journal of Oral and Maxillofacial Surgery. 2009;67(10):2254-65.	Excluded by title
79	Hamed-Sangsari A, Chinipardaz Z, Carrasco L. Following Surgically Assisted Rapid Palatal Expansion, Do Tooth-Borne or Bone-Borne Appliances Provide More Skeletal Expansion and Dental Expansion? J Oral Maxillofac Surg. 2017;75(10):2211-22.	Excluded by title
80	Hernández-Alfaro F, Guijarro-Martínez R, Peiró-Guijarro MA. Surgery first in orthognathic surgery: What have we learned? A comprehensive workflow based on 45 consecutive cases. Journal of Oral and Maxillofacial Surgery. 2014;72(2):376-90.	Excluded by title
81	Hernandez-Alfaro F, Mareque Bueno J, Diaz A, Pages CM. Minimally invasive surgically assisted rapid palatal expansion with limited approach under sedation: a report of 283 consecutive cases. J Oral Maxillofac Surg. 2010;68(9):2154-8.	Excluded by title
82	Hess D, Buser D, Dietschi D, Grossen G, Schonenberger A, Belzer UC. Esthetic single-tooth replacement with implants: a team approach. Quintessence Int. 1998;29(2):77-86.	Excluded by title
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413	Seo YJ, Lin L, Kim SH, Chung KR, Nelson G. Strategic camouflage treatment of skeletal Class III malocclusion (mandibular prognathism) using bone-borne rapid maxillary expansion and mandibular anterior subapical osteotomy. Am J Orthod Dentofacial Orthop. 2016;149(1):114-26.	Excluded; no dental-anchored expansion
414	Tausche E, Hansen L, Hietschold V, Lagravere MO, Harzer W. Three-dimensional evaluation of surgically assisted implant bone-borne rapid maxillary expansion: a pilot study. Am J Orthod Dentofacial Orthop. 2007;131(4 Suppl):S92-9.	Excluded; no dental-anchored expansion
415	Vassar JW, Karydis A, Trojan T, Fisher J. Dentoskeletal effects of a temporary skeletal anchorage device-supported rapid maxillary expansion appliance (TSADME): A pilot study. Angle Orthod. 2016;86(2):241-9.	Excluded; no dental-anchored expansion
416	Vassar JW, Karydis A, Trojan T, Fisher J. Dentoskeletal effects of a temporary skeletal anchorage device-supported rapid maxillary expansion appliance (TSADME): A pilot study. Angle Orthodontist. 2016;86(2):241-9.	Excluded; no dental-anchored expansion
417	Willmann JH, Nienkemper M, Becker K, Ihssen B, Wilmes B, Drescher D. The Hybrid Hyrax Distalizer - Skeletal Anchorage Device for Transversal and Sagittal Corrections in the Maxilla. Informationen Aus Orthodontie Und Kieferorthopaedie. 2016;48(4):228-36.	Excluded; no dental-anchored expansion
418	Wilmes B, Nienkemper M, Drescher D. Application and effectiveness of a mini-implant- and tooth-borne rapid palatal expansion device: the hybrid hyrax. World J Orthod. 2010;11(4):323-30.	Excluded; no dental-anchored expansion
419	Winsauer H, Vlachojannis J, Winsauer C, Ludwig B, Walter A. A bone-borne appliance for rapid maxillary expansion. J Clin Orthod. 2013;47(6):375-81; quiz 88.	Excluded; no dental-anchored expansion
420	Lin L, Ahn HW, Kim SJ, Moon SC, Kim SH, Nelson G. Tooth-borne vs bone-borne rapid maxillary expanders in late adolescence. Angle Orthod. 2015;85(2):253-62.	Excluded; retrospective study
421	Lin L, Ahn HW, Kim SJ, Moon SC, Kim SH, Nelson G. Tooth-borne vs bone-borne rapid maxillary expanders in late adolescence. Angle Orthodontist. 2015;85(2):253-62.	Excluded; retrospective study
422	Yilmaz A, Arman-Ozircipici A, Erken S, Polat-Ozsoy O. Comparison of short-term effects of mini-implant-supported maxillary expansion appliance with two conventional expansion protocols. Eur J Orthod. 2015;37(5):556-64.	Excluded; retrospective study
423	Yilmaz A, Arman-Ozircipici A, Erken S, Polat-Ozsoy O. Comparison of short-term effects of mini-implant-supported maxillary expansion appliance with two conventional expansion protocols. European Journal of Orthodontics. 2015;37(5):556-64.	Excluded; retrospective study
424	Mosleh MI, Kaddah MA, Abd ElSayed FA, ElSayed HS. Comparison of transverse changes during maxillary expansion with 4-point bone-borne and tooth-borne maxillary expanders. Am J Orthod Dentofacial Orthop. 2015;148(4):599-607.	Excluded; non-randomized
<b>Inclusion</b>		
425	Bazargani F, Magnuson A, Ludwig B. Effects on nasal airflow and resistance using two different RME appliances: a randomized controlled trial. Eur J Orthod. 2018;40(3):281-4.	Included; randomized
426	Canan S, Senisik NE. Comparison of the treatment effects of different rapid maxillary expansion devices on the maxilla and the mandible. Part 1: Evaluation of dentoalveolar changes. Am J Orthod Dentofacial Orthop. 2017;151(6):1125-38.	Included; randomized
427	Celenk-Koca T, Erdinc AE, Hazar S, Harris L, English JD, Akyalcin S. Evaluation of miniscrew-supported rapid maxillary expansion in adolescents: (A prospective randomized clinical trial). Angle Orthod 2018 [Epub ahead of print]	Included; randomized
428	Feldmann I, Bazargani F. Pain and discomfort during the first week of rapid maxillary expansion (RME) using two different RME appliances: A randomized controlled trial. Angle Orthod 2017;87(3):391-6.	Included; randomized
429	Gunyuz Toklu M, Germec-Cakan D, Tozlu M. Periodontal, dentoalveolar, and skeletal effects of tooth-borne and tooth-bone-borne expansion appliances. Am J Orthod Dentofacial Orthop. 2015;148(1):97-109.	Included; randomized
430	Kabalan O, Gordon J, Heo G, Lagravere MO. Nasal airway changes in bone-borne and tooth-borne rapid maxillary expansion treatments. Int Orthod. 2015;13(1):1-15.	Included; randomized

431	Lagravere MO, Carey J, Heo G, Toogood RW, Major PW. Transverse, vertical, and anteroposterior changes from bone-anchored maxillary expansion vs traditional rapid maxillary expansion: a randomized clinical trial. Am J Orthod Dentofacial Orthop. 2010;137(3):304.e1-12; discussion -5.	Included; randomized
432	Lagravere MO, Gamble J, Major PW, Heo G. Transverse dental changes after tooth-borne and bone-borne maxillary expansion. Int Orthod. 2013;11(1):21-34.	Included; randomized
433	Stepanko LS, Lagravère MO. Sphenoid bone changes in rapid maxillary expansion assessed with cone-beam computed tomography. Korean J Orthod 2016;46(5):269-79.	Included; randomized
434	Forst DD. External Root Resorption Associated with Maxillary Expansion Therapies as Evaluated via Cone Beam Computed Tomography: A Retrospective Randomized Clinical Trial. MSc Thesis, 2015, University of Alberta.	Included; randomized
435	Lagravere MOV. Analysis of Skeletal and Dental Changes with a Tooth-Borne and a Bone-Borne Maxillary Expansion Appliance assessed through Digital Volumetric Imaging. PhD Thesis, 2009, University of Alberta.	Included; randomized

**Appendix 4.** Details of the expansion appliances used in the included trials.

<b>Study</b>	<b>Bone anchorage (bone-borne or hybrid)</b>	<b>Tooth anchorage (tooth-borne)</b>
Bazargani 2018	<b>Hybrid RME</b> <ul style="list-style-type: none"> <li>▪ 2 x 1.7 x 8 mm mini-screw implants (Orthoeasy®; Forestadent, Pforzheim, Germany) at the anterior palate</li> <li>▪ 1<sup>st</sup> molar bands soldered to the expander</li> </ul>	<b>Tooth-borne RME</b> <ul style="list-style-type: none"> <li>▪ 1<sup>st</sup> molar bands soldered to the expander; extension arms at the 1<sup>st</sup> / 2<sup>nd</sup> primary molars</li> </ul>
Canan 2017	<b>Bone-borne RME</b> <ul style="list-style-type: none"> <li>▪ 4 x 1.8 x 9 mm pre-drilling mini-screw implants (Yesanchor; Seoul, Korea) at the palatal sides</li> </ul> <b>Hybrid RME</b> <ul style="list-style-type: none"> <li>▪ 2 x 1.8 x 9 mm pre-drilling mini-screw implants (Yesanchor; Seoul, Korea) at the posterior palate</li> <li>▪ 1<sup>st</sup> molar bands soldered to the expander</li> </ul>	<b>Tooth-borne RME</b> <ul style="list-style-type: none"> <li>▪ 1<sup>st</sup> premolar &amp; 1<sup>st</sup> molar bands connected and soldered to the expander</li> </ul>
Celenk-Koca 2018	<b>Bone-borne RME</b> <ul style="list-style-type: none"> <li>▪ 4 x 1.8 x 9 mm pre-drilling mini-screw implants (Orlus; Ortholution Co, Seoul, Korea) at the palatal sides</li> </ul>	<b>Tooth-borne RME</b> <ul style="list-style-type: none"> <li>▪ Cast expander on the 1<sup>st</sup> premolar, 2<sup>nd</sup> premolar, &amp; 1<sup>st</sup> molar with extension arm for the 2<sup>nd</sup> molar</li> </ul>
Feldmann 2017	<b>Hybrid RME</b> <ul style="list-style-type: none"> <li>▪ 2 x 1.7 x 8 mm mini-screw implants (Orthoeasy®; Forestadent, Pforzheim, Germany) at the anterior palate</li> <li>▪ 1<sup>st</sup> molar bands soldered to the expander</li> </ul>	<b>Tooth-borne RME</b> <ul style="list-style-type: none"> <li>▪ 1<sup>st</sup> molar bands soldered to the expander; extension arms at the 1<sup>st</sup> / 2<sup>nd</sup> primary molars</li> </ul>
Gunyuz Toklu 2015	<b>Hybrid RME</b> <ul style="list-style-type: none"> <li>▪ 2 x 1.8 x 9 mm mini-screw implants (Total Anchor; Trimed, Ankara, Turkey) at the anterior palate</li> <li>▪ 1<sup>st</sup> molar bands soldered to the expander</li> </ul>	<b>Tooth-borne RME</b> <ul style="list-style-type: none"> <li>▪ 1<sup>st</sup> premolar &amp; 1<sup>st</sup> molar bands connected and soldered to the expander</li> </ul>
Lagravere 2009 <sup>collated†</sup>	<b>Hybrid RME</b> <ul style="list-style-type: none"> <li>▪ 2 x onplants and 2 x 1.5 x 12 mm mini-screw implants (Straumann GBR-System; Andover, Mass) at the anterior palate</li> </ul>	<b>Tooth-borne RME</b> <ul style="list-style-type: none"> <li>▪ 1<sup>st</sup> premolar &amp; 1<sup>st</sup> molar bands connected and soldered to the expander</li> </ul>

RME, rapid maxillary expansion

## Appendix 5. Risk of bias assessment of included randomized trials.

Study	Sequence generation	Allocation concealment	Blinding of participants/ personnel	Blinding of outcome assessors	Incomplete outcome data	Selective outcome reporting	Other sources of bias
Bazargani 2018	<b>Low risk</b> - "Participants were randomly allocated in blocks of different sizes, using the concealed allocation principle in a 1:1 ratio, to two groups, a TB group and a TBB group. The randomization procedure was as follows: a computer-generated randomization list..."	<b>Low risk</b> – central allocation: "...and stored with a research secretary at the Postgraduate Dental Education Centre. Each time a patient gave his/her consent, the secretary was contacted by e-mail to provide the information about which type of expander the patient should receive."	<b>Low risk</b> – patients and treatment providers were not blinded, but treatment providers could have been. However, the outcome is objective and has been assessed blindly.	<b>Low risk</b> – "The intermolar measurements were blinded; the examiner was unaware of which treatment the patients had received or which models were taken at pre- and post-expansion. The care providers at the ENT unit who conducted all the rhinomanometry examinations were blinded to which group the patients were allocated to".	<b>Unclear</b> – double attrition rate for the more invasive group (33%) compared to the conventional group (16%); although imputation methods were used to assess the effect of attrition on the results, higher attrition might indicate lower tolerability of the intervention.	<b>Unclear</b> – no obvious selective reporting; however, only dental arch width is assessed and no dental inclination or skeletal width is assessed; finally, it is difficult to judge however whether selective reporting is a problem, as no protocol exists.	<b>Low risk</b> – no other sources of bias; intervention is dependent on patient compliance (which is not reported), but as treatment end was based on objective effects (expansion), this was considered irrelevant.
Canan 2017	<b>Unclear</b> - "Three study groups were designated with stratified randomization (strata, sex)..."	<b>Unclear</b> – No mention throughout the paper.	<b>Unclear</b> - Blinding of participants and personnel impossible; outcome is objective but it is unclear if assessed blindly.	<b>High risk</b> – No mention of blinding throughout the paper; blinding however is possible.	<b>Low risk</b> – 6 drop-outs (11%) after randomization (5 after treatment administration); although reasons for drop-outs might be related to treatment tolerability/acceptance, drop-out rate is relatively low.	<b>Unclear</b> – no obvious selective reporting; however, it is difficult to judge however whether selective reporting is a problem, as no protocol exists.	<b>Low risk</b> – no other sources of bias; intervention is dependent on patient compliance (which is not reported), but as treatment end was based on objective effects (expansion) and expansion duration is reported, this was considered irrelevant.
Celenk-Koca 2018	<b>Low risk</b> – "Patients were randomly assigned to one of the two treatment groups via a block randomization procedure with a block size of four, using a computer-generated list of random numbers".	<b>Low risk</b> – "The allocation sequence was concealed from the orthodontist, researchers, and the patients. When a patient was deemed as eligible for enrollment, the patient was assigned to a treatment group using opaque and sealed envelopes containing the allocation number."	<b>Low risk</b> - Blinding of participants and personnel impossible; outcome is objective and has been assessed and analyzed blindly.	<b>Low risk</b> – "Since it was impossible to blind the patient and orthodontist to the treatment groups, the researcher who traced the cone-beam computed tomography (CBCT) images and the statistician who evaluated the data were blinded".	<b>Low risk</b> – no drop outs.	<b>Low risk</b> – no obvious selective reporting; although it is difficult to judge however whether selective reporting is a problem, as no protocol exists, all possible dental/skeletal outcomes that could be measured by CBCT are reported.	<b>Low risk</b> – no other sources of bias; intervention is dependent on patient compliance (which is not reported), but as treatment end was based on objective effects (expansion), this was considered irrelevant.
Feldmann 2017	<b>Low risk</b> - "...a computer-generated randomization list was created using SPSS software (version 17.0; SPSS, Chicago, Ill) and stored with a research secretary at the Postgraduate Dental Education Centre"	<b>Low risk</b> – central allocation: "Each time a patient gave his/her consent, the secretary was contacted by e-mail and the information about which type of expander the patient should receive was acquired".	<b>Low risk</b> - Blinding of participants and personnel impossible; outcome is subjective but was assessed blindly.	<b>Low risk</b> – "The questionnaires were analyzed by one of the coauthors, who was blinded to the study and performed no orthodontic treatment on the patients."	<b>Low risk</b> – low drop-out rate (7%) which is transparently reported and balanced and the post-drop-out similarity is assessed.	<b>Low risk</b> – no obvious selective reporting; although it is difficult to judge however whether selective reporting is a problem, as no protocol exists, all possible patient-reported outcomes that could be measured within a trial with so short span (1 week) are reported.	<b>Unclear</b> –intervention (and probably outcome) is dependent on patient compliance (which is not reported) and no information given about patient compliance with given instructions.
Gunyuz Toklu 2015	<b>High risk</b> – randomization is unclear, but resembles more an alteration scheme: "According to the order of referral with a randomization ratio of 1:1, they were randomly allocated to 2 groups by an orthodontist (D.G.-C.) who did not know in advance which treatment the next patient would get."	<b>Low risk</b> – central allocation; see sequence generation text.	<b>Unclear</b> - Blinding of participants and personnel impossible; outcome is objective but it is unclear if assessed blindly.	<b>High risk</b> – No mention of blinding of outcome assessment, even though this is possible. Only measurement of the statistician, which is not equally important: "All measurements were made by the same researcher (M.G.T.). Blinding was used at the analysis level."	<b>Low risk</b> – Low drop-out rate (4%): "One patient who lost the palatal miniscrews 2 days after insertion of the expander because of consuming hard foods was excluded from the study."	<b>Unclear</b> – no obvious selective reporting; however, it is difficult to judge however whether selective reporting is a problem, as no protocol exists.	<b>Low risk</b> – no other sources of bias; intervention is dependent on patient compliance (which is not reported), but as treatment end was based on objective effects (expansion) and expansion duration is reported, this was considered irrelevant.
Lagravere 2009 <sup>collated†</sup>	<b>Low risk</b> - "...the subjects were randomized into the groups by using a random numbers generated list."	<b>Unclear</b> – No mention throughout the paper.	<b>Unclear</b> – Blinding of participants and personnel impossible; outcome is objective but it is unclear if assessed blindly.	<b>High risk</b> – No mention of blinding throughout the paper; blinding however is possible.	<b>Low risk</b> - No drop-outs or patient losses are reported.	<b>Unclear</b> – no obvious selective reporting; however, it is difficult to judge however whether selective reporting is a problem, as no protocol exists.	<b>Low risk</b> – no other sources of bias; intervention is dependent on patient compliance (which is not reported), but as treatment end was based on objective effects (expansion), this was considered irrelevant.

**Appendix 6a.** List of included trials comparing bone-borne with tooth-borne rapid maxillary expansion.

Outcome category	Trial	Outcome	Timing	MD	95% CI	P	Clinical relevance
Skeletal <sub>maxilla</sub>	Lagravere 2009	External maxilla width at 1 <sup>st</sup> molar	Pst-Exp	-0.53	-1.48, 0.42	0.27	-
Skeletal <sub>maxilla</sub>	Lagravere 2009	External maxilla width at 1 <sup>st</sup> premolar	Pst-Exp	-0.26	-1.41, 0.89	0.66	-
Skeletal <sub>maxilla</sub>	Lagravere 2009	External maxilla width at pterygoid	Pst-Exp	-0.39	-1.71, 0.93	0.56	-
Dental <sub>position</sub>	Canan 2017	Inter-canine width (cusp)	Pst-Exp	-0.70	-0.97, -0.43	<0.001	Yes
Dental <sub>position</sub>	Lagravere 2009	Inter-central-incisor width (apex)	Pst-Exp	-0.56	-1.65, 0.53	0.32	-
Dental <sub>position</sub>	Lagravere 2009	Inter-central-incisor width (pulp chamber)	Pst-Exp	-0.87	-1.77, 0.03	0.06	-
Dental <sub>position</sub>	Lagravere 2009	Intermolar width (apex)	Pst-Exp	0.08	-0.82, 0.98	0.86	-
Dental <sub>position</sub>	Canan 2017	Intermolar width (cusp)	Pst-Exp	-0.09	-0.34, 0.16	0.48	-
Dental <sub>position</sub>	Lagravere 2009	Intermolar width (pulp chamber)	Pst-Exp	-0.15	-1.30, 1.00	0.80	-
Dental <sub>position</sub>	Lagravere 2009	Inter-1 <sup>st</sup> -premolar width (apex)	Pst-Exp	-0.52	-1.53, 0.49	0.31	-
Dental <sub>position</sub>	Canan 2017	Inter-1 <sup>st</sup> -premolar width (cusp)	Pst-Exp	0.23	-0.15, 0.61	0.23	-
Dental <sub>position</sub>	Lagravere 2009	Inter-1 <sup>st</sup> -premolar width (pulp chamber)	Pst-Exp	-1.80	-2.92, -0.68	0.002	No
Dental <sub>inclination</sub>	Canan 2017	Inclination 1 <sup>st</sup> molar (left)	Pst-Exp	-5.39	-8.04, -2.74	<0.001	Yes
Dental <sub>inclination</sub>	Lagravere 2009	Inclination 1 <sup>st</sup> molar (left)	Pst-Exp	-0.35	-3.40, 2.70	0.82	-
Dental <sub>inclination</sub>	Canan 2017	Inclination 1 <sup>st</sup> molar (right)	Pst-Exp	-2.12	-5.46, 1.22	0.21	-
Dental <sub>inclination</sub>	Lagravere 2009	Inclination 1 <sup>st</sup> molar (right)	Pst-Exp	-0.76	-4.27, 2.75	0.67	-
Dental <sub>inclination</sub>	Canan 2017	Inclination 1 <sup>st</sup> premolar (left)	Pst-Exp	-4.03	-6.79, -1.27	0.004	No
Dental <sub>inclination</sub>	Lagravere 2009	Inclination 1 <sup>st</sup> premolar (left)	Pst-Exp	-1.25	-3.33, 0.83	0.24	-
Dental <sub>inclination</sub>	Canan 2017	Inclination 1 <sup>st</sup> premolar (right)	Pst-Exp	-4.28	-6.92, -1.64	0.001	Yes
Dental <sub>inclination</sub>	Lagravere 2009	Inclination 1 <sup>st</sup> premolar (right)	Pst-Exp	-3.79	-6.60, -0.98	0.008	No
Nasal cavity	Lagravere 2009	Nasal cavity width at orbita	Pst-Exp	0.24	-0.13, 0.61	0.20	-
Cranial <sub>vertical</sub>	Lagravere 2009	Height orbita-incisor (left)	Pst-Exp	-0.50	-1.79, 0.79	0.45	-
Cranial <sub>vertical</sub>	Lagravere 2009	Height orbita-incisor (right)	Pst-Exp	-1.40	-2.48, -0.32	0.01	No
Cranial <sub>vertical</sub>	Lagravere 2009	Height orbita-1 <sup>st</sup> molar (left)	Pst-Exp	0.02	-1.53, 1.57	0.98	-
Cranial <sub>vertical</sub>	Lagravere 2009	Height orbita-1 <sup>st</sup> molar (right)	Pst-Exp	-0.38	-1.36, 0.60	0.45	-
Cranial <sub>vertical</sub>	Lagravere 2009	Height orbita-menton (left)	Pst-Exp	-0.67	-2.58, 1.24	0.49	-
Cranial <sub>vertical</sub>	Lagravere 2009	Height orbita-menton (right)	Pst-Exp	-0.80	-1.68, 1.08	0.40	-
Mandible	Lagravere 2009	Lower intermolar width (pulpal chamber)	Pst-Exp	-0.56	-1.28, 0.16	0.13	-
Mandible	Lagravere 2009	Mandible width at foramen	Pst-Exp	0.30	-0.07, 0.67	0.11	-
Skeletal <sub>maxilla</sub>	Celenk-Koca 2018	Buccal bone thickness at 1 <sup>st</sup> molar	Reten	0.14	0.04, 0.24	0.005	No
Skeletal <sub>maxilla</sub>	Celenk-Koca 2018	Buccal bone thickness at 1 <sup>st</sup> premolar	Reten	0.25	0.13, 0.37	<0.001	Yes
Skeletal <sub>maxilla</sub>	Celenk-Koca 2018	Incisal foramen width	Reten	1.80	1.27, 2.33	<0.001	Yes
Skeletal <sub>maxilla</sub>	Lagravere 2009	External maxilla width at 1 <sup>st</sup> molar	Reten	-0.70	-1.83, 0.43	0.22	-
Skeletal <sub>maxilla</sub>	Lagravere 2009	External maxilla width at 1 <sup>st</sup> premolar	Reten	-1.01	-2.23, 0.21	0.22	-
Skeletal <sub>maxilla</sub>	Lagravere 2009	External maxilla width at pterygoid	Reten	-0.33	-1.71, 1.05	0.11	-
Skeletal <sub>maxilla</sub>	Celenk-Koca 2018	Parallel suture opening	Reten	*2.50	*0.55, 11.41	0.24	-
Skeletal <sub>maxilla</sub>	Celenk-Koca 2018	Suture width at 1 <sup>st</sup> molar	Reten	2.00	1.40, 2.60	<0.001	Yes
Skeletal <sub>maxilla</sub>	Celenk-Koca 2018	Suture width at 1 <sup>st</sup> premolar	Reten	2.30	1.69, 2.91	<0.001	Yes
Dental <sub>position</sub>	Lagravere 2009	Inter-central-incisor width (apex)	Reten	-0.33	-1.26, 0.60	0.49	-
Dental <sub>position</sub>	Lagravere 2009	Inter-central-incisor width (pulpal chamber)	Reten	-0.11	-0.67, 0.45	0.70	-
Dental <sub>position</sub>	Canan 2017	Inter-canine width (cusp)	Reten	-0.51	-0.95, -0.07	0.02	Yes

Dental <sub>position</sub>	Lagravere 2009	Intermolar width (apex)	Reten	-0.71	-1.87, 0.45	0.23	-
Dental <sub>position</sub>	Canan 2017	Intermolar width (cusp)	Reten	0.15	-0.36, 0.66	0.57	-
Dental <sub>position</sub>	Celenk-Koca 2018	Intermolar width (palatal crown middle)	Reten	0.30	-0.64, 1.24	0.53	-
Dental <sub>position</sub>	Lagravere 2009	Intermolar width (pulpal chamber)	Reten	-0.08	-1.16, 1.00	0.89	-
Dental <sub>position</sub>	Lagravere 2009	Inter-1 <sup>st</sup> -premolar width (apex)	Reten	-1.81	-3.07, -0.55	0.005	No
Dental <sub>position</sub>	Canan 2017	Inter-1 <sup>st</sup> -premolar width (cusp)	Reten	-0.39	-1.07, 0.29	0.26	-
Dental <sub>position</sub>	Celenk-Koca 2018	Inter-1 <sup>st</sup> -premolar width (palatal crown middle)	Reten	0.60	-1.18, 2.38	0.51	-
Dental <sub>position</sub>	Lagravere 2009	Inter-1 <sup>st</sup> -premolar width (pulpal chamber)	Reten	-1.76	-2.66, -0.86	<0.001	Yes
Dental <sub>inclination</sub>	Celenk-Koca 2018	Inclination 1 <sup>st</sup> molar (right-left average)	Reten	-5.20	-6.95, -3.45	<0.001	Yes
Dental <sub>inclination</sub>	Canan 2017	Inclination 1 <sup>st</sup> molar (left)	Reten	-5.83	-9.98, -1.68	0.006	Yes
Dental <sub>inclination</sub>	Lagravere 2009	Inclination 1 <sup>st</sup> molar (left)	Reten	1.92	-1.74, 5.58	0.30	-
Dental <sub>inclination</sub>	Canan 2017	Inclination 1 <sup>st</sup> molar (right)	Reten	-2.38	-6.30, 1.54	0.23	-
Dental <sub>inclination</sub>	Lagravere 2009	Inclination 1 <sup>st</sup> molar (right)	Reten	1.44	-1.28, 4.16	0.30	-
Dental <sub>inclination</sub>	Celenk-Koca 2018	Inclination 1 <sup>st</sup> premolar (right-left average)	Reten	-5.10	-6.78, -3.42	<0.001	Yes
Dental <sub>inclination</sub>	Canan 2017	Inclination 1 <sup>st</sup> premolar (left)	Reten	-6.21	-10.13, -2.30	0.002	No
Dental <sub>inclination</sub>	Lagravere 2009	Inclination 1 <sup>st</sup> premolar (left)	Reten	1.09	-1.25, 3.43	0.36	-
Dental <sub>inclination</sub>	Canan 2017	Inclination 1 <sup>st</sup> premolar (right)	Reten	-1.39	-5.17, 2.39	0.47	-
Dental <sub>inclination</sub>	Lagravere 2009	Inclination 1 <sup>st</sup> premolar (right)	Reten	-0.43	-3.24, 2.38	0.76	-
Nasal cavity	Lagravere 2009	Nasal cavity width (cross-section 1; left)	Reten	-0.02	-0.06, 0.02	0.36	-
Nasal cavity	Lagravere 2009	Nasal cavity width (cross-section 1; right)	Reten	0.02	-0.04, 0.08	0.48	-
Nasal cavity	Lagravere 2009	Nasal cavity width (cross-section 2; left)	Reten	1.04	-0.87, 2.95	0.29	-
Nasal cavity	Lagravere 2009	Nasal cavity width (cross-section 2; right)	Reten	0.02	-0.03, 0.07	0.39	-
Nasal cavity	Lagravere 2009	Nasal cavity volume 1 (left)	Reten	0.42	-0.25, 1.09	0.22	-
Nasal cavity	Lagravere 2009	Nasal cavity volume 1 (right)	Reten	0.39	-0.31, 1.09	0.27	-
Nasal cavity	Lagravere 2009	Nasal cavity volume 2 (left)	Reten	0.15	-0.54, 0.84	0.67	-
Nasal cavity	Lagravere 2009	Nasal cavity volume 2 (right)	Reten	0.68	-0.91, 2.27	0.40	-
Nasal cavity	Celenk-Koca 2018	Nasal cavity width at 1 <sup>st</sup> molar	Reten	1.70	0.81, 2.59	<0.001	Yes
Nasal cavity	Lagravere 2009	Nasal cavity width at orbita	Reten	0.17	-0.24, 0.58	0.42	-
Nasal cavity	Celenk-Koca 2018	Nasal cavity width at 1 <sup>st</sup> premolar	Reten	1.00	-0.09, 2.09	0.07	-
Cranial <sub>vertical</sub>	Lagravere 2009	Height orbita-incisor (left)	Reten	-0.18	-0.96, 0.60	0.65	-
Cranial <sub>vertical</sub>	Lagravere 2009	Height orbita-incisor (right)	Reten	-0.51	-1.17, 0.15	0.13	-
Cranial <sub>vertical</sub>	Lagravere 2009	Height orbita-1 <sup>st</sup> molar (left)	Reten	0.40	-0.32, 1.12	0.27	-
Cranial <sub>vertical</sub>	Lagravere 2009	Height orbita-1 <sup>st</sup> molar (right)	Reten	0.25	-0.51, 1.01	0.52	-
Cranial <sub>vertical</sub>	Lagravere 2009	Height orbita-menton (left)	Reten	0.03	-0.91, 0.97	0.95	-
Cranial <sub>vertical</sub>	Lagravere 2009	Height orbita-menton (right)	Reten	0.05	-1.01, 1.11	0.93	-
Mandible	Lagravere 2009	Lower intermolar width (pulpal chamber)	Reten	-0.20	-0.72, 0.32	0.45	-
Mandible	Lagravere 2009	Mandible width at foramen	Reten	0.20	-0.19, 0.59	0.31	-
Root resorption	Celenk-Koca 2018	Root resorption linear (1 <sup>st</sup> molar mesiobuccal root)	Reten	0.06	-0.04, 0.16	0.23	-
Root resorption	Celenk-Koca 2018	Root resorption linear (1 <sup>st</sup> molar mesiodistal root)	Reten	-0.07	-0.19, 0.05	0.27	-
Root resorption	Celenk-Koca 2018	Root resorption linear (1 <sup>st</sup> molar palatal root)	Reten	0.07	-0.03, 0.17	0.16	-
Root resorption	Celenk-Koca 2018	Root resorption linear (1 <sup>st</sup> premolar buccal root)	Reten	0.13	0.01, 0.25	0.04	No

Root resorption	Celenk-Koca 2018	Root resorption linear (1 <sup>st</sup> premolar palatal root)	Reten	0.09	-0.05, 0.23	0.20	-
Root resorption	Lagravere 2009	Root resorption volume (1 <sup>st</sup> molar)	Reten	-17.82	-46.01, 10.37	0.22	-
Root resorption	Lagravere 2009	Root resorption % volume (1 <sup>st</sup> molar)	Reten	-1.51	-3.91, 0.89	0.22	-

CI, confidence interval; MD, mean difference; Pst-Exp, post expansion; Reten, post retention period (at least 3 months).

\* pertains to risks and not mean difference.

Judged arbitrarily as mean difference being equal or greater to one standard deviation of the control group.

**Appendix 6b.** List of included trials comparing hybrid (tooth-bone-borne) with tooth-borne rapid maxillary expansion.

Outcome category	Trial	Outcome	Timing	MD	95% CI	P	Cl rel
Pain	Feldmann 2017	Analgesic use on day 4	Mid-Exp	*0.78	*0.34, 1.76	0.55	-
Pain	Feldmann 2017	Analgesic use on day 4	Mid-Exp	*0.40	*0.09, 1.87	0.25	-
Dental <sub>position</sub>	Canan 2017	Inter canine width (cusp)	Pst-Exp	-0.68	-0.94, -0.42	<0.001	Yes
Dental <sub>position</sub>	Canan 2017	Inter molar width (cusp)	Pst-Exp	-0.06	-0.36, 0.24	0.69	-
Dental <sub>position</sub>	Canan 2017	Inter-1 <sup>st</sup> -premolar width (cusp)	Pst-Exp	0.14	-0.28, 0.56	0.52	-
Dental <sub>inclination</sub>	Canan 2017	Inclination 1 <sup>st</sup> molar (left)	Pst-Exp	-1.45	-4.03, 1.13	0.27	-
Dental <sub>inclination</sub>	Canan 2017	Inclination 1 <sup>st</sup> molar (right)	Pst-Exp	3.20	-0.62, 7.02	0.10	-
Dental <sub>inclination</sub>	Canan 2017	Inclination 1 <sup>st</sup> premolar (left)	Pst-Exp	-3.31	-6.85, 0.23	0.07	-
Dental <sub>inclination</sub>	Canan 2017	Inclination 1 <sup>st</sup> premolar (right)	Pst-Exp	-1.16	-4.32, 2.00	0.47	-
Nasal cavity	Bazargani 2018	Nasal airflow	Pst-Exp	57.70	1.44, 113.96	0.04	No
Nasal cavity	Bazargani 2018	Nasal resistance	Pst-Exp	-0.23	-0.43, -0.04	0.02	No
Skeletal <sub>maxilla</sub>	Gunyuz Toklu 2015	Buccal bone thickness at canine (left)	Reten	-0.25	-0.63, 0.13	0.20	-
Skeletal <sub>maxilla</sub>	Gunyuz Toklu 2015	Buccal bone thickness at canine (right)	Reten	0.00	-0.28, 0.28	1.00	-
Skeletal <sub>maxilla</sub>	Gunyuz Toklu 2015	Buccal bone thickness at 1 <sup>st</sup> molar (averaged)	Reten	-0.15	-0.66, 0.36	0.56	-
Skeletal <sub>maxilla</sub>	Gunyuz Toklu 2015	Buccal bone thickness at 1 <sup>st</sup> molar (distobuccal root; left)	Reten	-0.21	-0.65, 0.23	0.35	-
Skeletal <sub>maxilla</sub>	Gunyuz Toklu 2015	Buccal bone thickness at 1 <sup>st</sup> molar (distobuccal root; right)	Reten	-0.13	-0.77, 0.51	0.69	-
Skeletal <sub>maxilla</sub>	Gunyuz Toklu 2015	Buccal bone thickness at 1 <sup>st</sup> molar (mesiobuccal root; left)	Reten	-0.11	-0.64, 0.42	0.69	-
Skeletal <sub>maxilla</sub>	Gunyuz Toklu 2015	Buccal bone thickness at 1 <sup>st</sup> molar (mesiobuccal root; right)	Reten	-0.15	-0.58, 0.28	0.49	-
Skeletal <sub>maxilla</sub>	Gunyuz Toklu 2015	Buccal bone thickness at 1 <sup>st</sup> premolar (averaged)	Reten	0.63	0.10, 1.16	0.02	Yes
Skeletal <sub>maxilla</sub>	Gunyuz Toklu 2015	Buccal bone thickness at 1 <sup>st</sup> premolar (left)	Reten	0.79	0.30, 1.28	0.001	Yes
Skeletal <sub>maxilla</sub>	Gunyuz Toklu 2015	Buccal bone thickness at 1 <sup>st</sup> premolar (right)	Reten	0.46	-0.13, 1.05	0.13	-
Skeletal <sub>maxilla</sub>	Gunyuz Toklu 2015	Buccal bone thickness at 2 <sup>nd</sup> premolar (left)	Reten	0.15	-0.32, 0.62	0.53	-
Skeletal <sub>maxilla</sub>	Gunyuz Toklu 2015	Buccal bone thickness at 2 <sup>nd</sup> premolar (right)	Reten	-0.11	-0.42, 0.20	0.49	-
Skeletal <sub>maxilla</sub>	Gunyuz Toklu 2015	Buccal bone thickness at canine (left)	Reten	-0.31	-0.96, 0.34	0.35	-
Skeletal <sub>maxilla</sub>	Gunyuz Toklu 2015	Buccal bone thickness at canine (right)	Reten	-0.03	-0.72, 0.66	0.93	-
Skeletal <sub>maxilla</sub>	Gunyuz Toklu 2015	Palatal bone thickness at 1 <sup>st</sup> molar (left)	Reten	0.04	-0.61, 0.69	0.90	-
Skeletal <sub>maxilla</sub>	Gunyuz Toklu 2015	Palatal bone thickness at 1 <sup>st</sup> molar (right)	Reten	-0.43	-0.95, 0.09	0.10	-
Skeletal <sub>maxilla</sub>	Gunyuz Toklu 2015	Palatal bone thickness at 1 <sup>st</sup> premolar (left)	Reten	-1.62	-2.21, -1.03	<0.001	Yes
Skeletal <sub>maxilla</sub>	Gunyuz Toklu 2015	Palatal bone thickness at 1 <sup>st</sup> premolar (right)	Reten	-0.61	-1.55, 0.33	0.20	-
Skeletal <sub>maxilla</sub>	Gunyuz Toklu 2015	Palatal bone thickness at 2 <sup>nd</sup> premolar (left)	Reten	-0.17	-0.67, 0.33	0.51	-
Skeletal <sub>maxilla</sub>	Gunyuz Toklu 2015	Palatal bone thickness at 2 <sup>nd</sup> premolar (right)	Reten	-0.66	-1.25, -0.07	0.03	No
Skeletal <sub>maxilla</sub>	Gunyuz Toklu 2015	External maxilla width at 1 <sup>st</sup> molar	Reten	0.64	-1.41 2.69	0.54	-
Skeletal <sub>maxilla</sub>	Gunyuz Toklu 2015	Palatal maxilla width at 1 <sup>st</sup> molar	Reten	-0.47	-2.29, 1.35	0.61	-



Skeletal <sub>maxilla</sub>	Gunyuz Toklu 2015	External maxilla width at pterygoid	Reten	0.14	-1.09, 1.37	0.82	-
Dental <sub>position</sub>	Gunyuz Toklu 2015	Intercanine width (apex)	Reten	1.69	-0.71, 4.09	0.17	-
Dental <sub>position</sub>	Canan 2017	Intercanine width (cusp)	Reten	-0.01	-0.37, 0.35	0.96	-
Dental <sub>position</sub>	Gunyuz Toklu 2015	Intercanine width (cusp)	Reten	-0.95	-2.39, 0.49	0.19	-
Dental <sub>position</sub>	Gunyuz Toklu 2015	Intermolar width (apex)	Reten	-1.69	-4.39, 1.01	0.22	-
Dental <sub>position</sub>	Canan 2017	Intermolar width (cusp)	Reten	0.14	-0.46, 0.74	0.65	-
Dental <sub>position</sub>	Gunyuz Toklu 2015	Intermolar width (mesiobuccal cusp)	Reten	0.57	-1.38, 2.52	0.57	-
Dental <sub>position</sub>	Gunyuz Toklu 2015	Intermolar width (averaged cusp)	Reten	0.54	-1.38, 2.46	0.58	-
Dental <sub>position</sub>	Gunyuz Toklu 2015	Intermolar width (distobuccal cusp)	Reten	0.52	-1.37, 2.41	0.59	-
Dental <sub>position</sub>	Gunyuz Toklu 2015	Inter-1 <sup>st</sup> -premolar width (apex)	Reten	-3.06	-5.73, -0.39	0.03	No
Dental <sub>position</sub>	Canan 2017	Inter-1 <sup>st</sup> -premolar width (cusp)	Reten	0.00	-0.69, 0.69	1.00	-
Dental <sub>position</sub>	Gunyuz Toklu 2015	Inter-1 <sup>st</sup> -premolar width (buccal cusp)	Reten	-4.33	-7.04, -1.62	0.002	Yes
Dental <sub>position</sub>	Gunyuz Toklu 2015	Inter-1 <sup>st</sup> -premolar width (palatal cusp)	Reten	-5.29	-7.81, -2.77	<0.001	Yes
Dental <sub>position</sub>	Gunyuz Toklu 2015	Inter-2 <sup>nd</sup> -premolar width (apex)	Reten	-0.38	-3.00, 2.24	0.78	-
Dental <sub>position</sub>	Gunyuz Toklu 2015	Inter-2 <sup>nd</sup> -premolar width (buccal cusp)	Reten	-3.33	-6.15, -0.51	0.02	Yes
Dental <sub>position</sub>	Gunyuz Toklu 2015	Inter-2 <sup>nd</sup> -premolar width (palatal cusp)	Reten	-3.48	-6.38, -0.58	0.02	No
Bone <sub>inclination</sub>	Gunyuz Toklu 2015	Alveolar inclination at 1 <sup>st</sup> molar (left)	Reten	-1.02	-5.16, 3.12	0.63	-
Bone <sub>inclination</sub>	Gunyuz Toklu 2015	Alveolar inclination at 1 <sup>st</sup> molar (right)	Reten	-0.35	-4.57, 3.87	0.87	-
Bone <sub>inclination</sub>	Gunyuz Toklu 2015	Alveolar inclination at 1 <sup>st</sup> premolar (left)	Reten	-1.48	-5.00, 2.04	0.41	-
Bone <sub>inclination</sub>	Gunyuz Toklu 2015	Alveolar inclination at 1 <sup>st</sup> premolar (right)	Reten	-1.04	-6.74, 4.66	0.72	-
Dental <sub>inclination</sub>	Gunyuz Toklu 2015	Absolute inclination 1 <sup>st</sup> molar (left)	Reten	0.95	-2.80, 4.70	0.62	-
Dental <sub>inclination</sub>	Gunyuz Toklu 2015	Absolute inclination 1 <sup>st</sup> molar (right)	Reten	-3.99	-8.75, 0.77	0.10	-
Dental <sub>inclination</sub>	Gunyuz Toklu 2015	Absolute inclination 1 <sup>st</sup> premolar (left)	Reten	-1.30	-3.55, 0.95	0.26	-
Dental <sub>inclination</sub>	Gunyuz Toklu 2015	Absolute inclination 1 <sup>st</sup> premolar (right)	Reten	-0.14	-5.60, 5.32	0.96	-
Dental <sub>inclination</sub>	Gunyuz Toklu 2015	Inclination canine (left)	Reten	-3.58	-8.51, 1.35	0.15	-
Dental <sub>inclination</sub>	Gunyuz Toklu 2015	Inclination canine (right)	Reten	0.48	-3.72, 4.68	0.82	-
Dental <sub>inclination</sub>	Canan 2017	Inclination 1 <sup>st</sup> molar (left)	Reten	-2.41	-5.63, 0.81	0.14	-
Dental <sub>inclination</sub>	Gunyuz Toklu 2015	Inclination 1 <sup>st</sup> molar (left)	Reten	-0.07	-3.42, 3.28	0.97	-
Dental <sub>inclination</sub>	Canan 2017	Inclination 1 <sup>st</sup> molar (right)	Reten	1.64	2.63, 5.91	0.45	-
Dental <sub>inclination</sub>	Gunyuz Toklu 2015	Inclination 1 <sup>st</sup> molar (right)	Reten	-4.34	-9.71, 1.03	0.11	-
Dental <sub>inclination</sub>	Canan 2017	Inclination 1 <sup>st</sup> premolar (left)	Reten	-6.09	-10.17, -2.01	0.003	No
Dental <sub>inclination</sub>	Gunyuz Toklu 2015	Inclination 1 <sup>st</sup> premolar (left)	Reten	-2.78	-4.96, -0.61	0.01	No
Dental <sub>inclination</sub>	Canan 2017	Inclination 1 <sup>st</sup> premolar (right)	Reten	-0.06	-4.16, 4.04	0.98	-
Dental <sub>inclination</sub>	Gunyuz Toklu 2015	Inclination 1 <sup>st</sup> premolar (right)	Reten	-1.17	-4.11, 1.77	0.44	-
Dental <sub>inclination</sub>	Gunyuz Toklu 2015	Inclination 2 <sup>nd</sup> premolar (left)	Reten	-1.48	-6.39, 3.43	0.55	-
Dental <sub>inclination</sub>	Gunyuz Toklu 2015	Inclination 2 <sup>nd</sup> premolar (right)	Reten	1.41	-2.04, 4.86	0.42	-
Nasal cavity	Gunyuz Toklu 2015	Nasal cavity width	Reten	0.08	-1.35, 1.51	0.91	-

CI, confidence interval; MD, mean difference; Pst-Exp, post expansion; Reten, post retention period (at least 3 months).

\* pertains to risks and not mean difference.

Judged arbitrarily as mean difference being equal or greater to one standard deviation of the control group.